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Term	Documents
GCSF	169
GCSFS	1
RECEPTOR	70543
RECEPTORS	37269
(GCSF ADJ RECEPTOR) AND 1	1

Database: [All Databases \(USPT + EPAB + JPAB + DWPI + TDBD\)](#)

11 and gcsf receptor

Refine Search:

**Search History**

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
ALL	11 and gcsf receptor	1	<u>L2</u>
ALL	11-3 or il3 or 11-7 or il7 or erythropoietin receptor or gcsf receptor or gcsf receptor	495	<u>L1</u>

**WEST**[Help](#)[Logout](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)**Search Results - Record(s) 1 through 1 of 1 returned.**

1. Document ID: ES 2134771 T3, WO 9114776 A, AU 9174968 A, JP 03505860 X, EP 521156 A1, EP 521156 A4, US 5574136 A, EP 521156 B1, DE 69131421 E

Entry 1 of 1

File: DWPI

Oct 16, 1999

DERWENT-ACC-NO: 1991-310576

DERWENT-WEEK: 199950

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TITLE: DNA encoding granulocyte colony stimulating factor  
receptor - for recombinant prodn. of GCSF receptor useful in  
therapy and research

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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Term	Documents
GCSF	169
GCSFS	1
RECEPTOR	70543
RECEPTORS	37269
(GCSF ADJ RECEPTOR) AND 1	1

[Display 20 Documents](#)

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[1](#)**Display Format:**[TI](#)[Change Format](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)[Help](#)[Logout](#)

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<a href="#">Full</a>	<a href="#">Title</a>	<a href="#">Citation</a>	<a href="#">Front</a>	<a href="#">Review</a>	<a href="#">Classification</a>	<a href="#">Date</a>	<a href="#">Reference</a>	<a href="#">Claims</a>	<a href="#">RWC</a>
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## Document Number 1

Entry 1 of 1

File: DWPI

Oct 16, 1999

DERWENT-ACC-NO: 1991-310576

DERWENT-WEEK: 199950

COPYRIGHT 2000 DERWENT INFORMATION LTD

TITLE: DNA encoding granulocyte colony stimulating factor receptor - for recombinant prodn. of GCSE receptor useful in therapy and research

INVENTOR: FUKUNAGA, R; NAGATA, S

PATENT-ASSIGNEE: OSAKA BIOSCIENCE INST[OSABN], OSAKA BIOSCIENCE INST[OSABN]

### PRIORITY-DATA:

APPL-NO

APPL-DATE

1990JP-0176629

July 3, 1990

1990JP-0074539

March 23, 1990

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
ES 2134771 T3	October 16, 1999	N/A	000	C07K014/00
WO 9114776 A	October 3, 1991	N/A	099	N/A
AU 9174968 A	October 21, 1991	N/A	000	N/A
JP 03505860 X	May 7, 1992	N/A	099	C12N015/12
EP 521156 A1	January 7, 1993	E	037	C12N015/12
EP 521156 A4	February 17, 1993	N/A	000	N/A
US 5574136 A	November 12, 1996	N/A	053	C12N015/12
EP 521156 B1	July 7, 1999	E	000	C07K014/00
DE 69131421 E	August 12, 1999	N/A	000	C07K014/00

DESIGNATED-STATES: AU BB BG BR CA FI HU JP KR LK MC MR MW NO PL RO SD SU US AT BE CH DE DK ES FR GB GR IT LU NL

OA SE AT BE CH DE DK ES FR GB GR IT LI LU NL SE AT BE CH  
DE DK ES FR GB GR IT LI LU NL SE

CITED-DOCUMENTS:3.Jnl.Ref; 2.Jnl.Ref ; WO 9105046

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
ES 2134771T3	March 22, 1991	1991EP-0905894	N/A
ES 2134771T3	N/A	EP 521156	Based on
JP 03505860X	March 22, 1991	1991JP-0505860	N/A
JP 03505860X	March 22, 1991	1991WO-JP00375	N/A
JP 03505860X	N/A	WO 9114776	Based on
EP 521156A1	March 22, 1991	1991EP-0905894	N/A
EP 521156A1	March 22, 1991	1991WO-JP00375	N/A
EP 521156A1	N/A	WO 9114776	Based on
EP 521156A4	N/A	1991EP-0905894	N/A
US 5574136A	March 22, 1991	1991WO-JP00375	N/A
US 5574136A	September 22, 1992	1992US-0923976	N/A
US 5574136A	N/A	WO 9114776	Based on
EP 521156B1	March 22, 1991	1991EP-0905894	N/A
EP 521156B1	March 22, 1991	1991WO-JP00375	N/A
EP 521156B1	N/A	WO 9114776	Based on
DE 69131421E	March 22, 1991	1991DE-0631421	N/A
DE 69131421E	March 22, 1991	1991EP-0905894	N/A
DE 69131421E	March 22, 1991	1991WO-JP00375	N/A
DE 69131421E	N/A	EP 521156	Based on
DE 69131421E	N/A	WO 9114776	Based on

INT-CL (IPC): C07K 13/00; C07K 14/00; C07K 14/705; C07K 14/715; C12N 5/10; C12N 15/12 ; C12P 21/02; C12R 1/91; C12P 21/02; C12R 1/19; C12P 21/02; C12R 1/19; C12P 21/02; C12R 1/91

ABSTRACTED-PUB-NO: EP 521156B  
BASIC-ABSTRACT:

The DNA sequence coding for granulocyte colony stimulating factor (GCSF) receptor is new. The sequence is pref. mouse of human in origin. The sequence may code

for all or part of the GCSF receptor amino acid sequence. The 2513-base DNA sequence and a 749 amino acid sequence that it codes are specifically claimed, as well as a vector and a transformant containing the DNA sequence and a method of producing the GCSF.

USE/ADVANTAGE - The murine DNA sequence is used as a probe to obtain human GCSF receptor sequence. By hybridisation with human histiocytic lymphoma, human acute myelogenous leukaemia, human promyelocyte leukaemia and human amnion of cell lines ATCG CRL 1593, CCL246, CCL240 and CCL62, the sequence can be produced for chemical use, study and research.

ABSTRACTED-PUB-NO: US 5574136A  
EQUIVALENT-ABSTRACTS:

The DNA sequence coding for granulocyte colony stimulating factor (GCSF) receptor is new. The sequence is pref. mouse of human in origin. The sequence may code for all or part of the GCSF receptor amino acid sequence. The 2513-base DNA sequence and a 749 amino acid sequence that it codes are specifically claimed, as well as a vector and a transformant containing the DNA sequence and a method of producing the GCSF.

USE/ADVANTAGE - The murine DNA sequence is used as a probe to obtain human GCSF receptor sequence. By hybridisation with human histiocytic lymphoma, human acute myelogenous leukaemia, human promyelocyte leukaemia and human amnion of cell lines ATCG CRL 1593, CCL246, CCL240 and CCL62, the sequence can be produced for chemical use, study and research.

An isolated DNA encoding murine G-CSF receptor which encodes the 837 residue amino acid sequence given in the specification, is new.

WO 9114776A

CHOSEN-DRAWING: Dwg.0/14 Dwg.0/21

DERWENT-CLASS: B04 D16

CPI-CODES: B04-B04A1; B04-B04A3; B04-B04H; B11-C07B5;  
B12-K04A; D05-C12; D05-H12;

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Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC
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**WEST**[Help](#)[Logout](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)**Search Results - Record(s) 1 through 14 of 14 returned.****1. Document ID: US 6028176 A**

Entry 1 of 14

File: USPT

Feb 22, 2000

US-PAT-NO: 6028176

DOCUMENT-IDENTIFIER: US 6028176 A

TITLE: High-affinity interleukin-4 muteins

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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**2. Document ID: US 5998598 A**

Entry 2 of 14

File: USPT

Dec 7, 1999

US-PAT-NO: 5998598

DOCUMENT-IDENTIFIER: US 5998598 A

TITLE: Immunoadhesins and methods of production and use thereof

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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**3. Document ID: US 5986059 A**

Entry 3 of 14

File: USPT

Nov 16, 1999

US-PAT-NO: 5986059

DOCUMENT-IDENTIFIER: US 5986059 A

TITLE: T-cell selective interleukin-4 agonists

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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**4. Document ID: US 5919456 A**

Entry 4 of 14

File: USPT

Jul 6, 1999

US-PAT-NO: 5919456

DOCUMENT-IDENTIFIER: US 5919456 A

TITLE: IL-13 receptor specific chimeric proteins

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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**5. Document ID: US 5866760 A**

Entry 5 of 14

File: USPT

Feb 2, 1999

US-PAT-NO: 5866760

DOCUMENT-IDENTIFIER: US 5866760 A

TITLE: Stat6 deficient transgenic mice

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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## 6. Document ID: US 5858701 A

Entry 6 of 14

File: USPT

Jan 12, 1999

US-PAT-NO: 5858701

DOCUMENT-IDENTIFIER: US 5858701 A

TITLE: DNA encoding an insulin receptor substrate

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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## 7. Document ID: US 5830453 A

Entry 7 of 14

File: USPT

Nov 3, 1998

US-PAT-NO: 5830453

DOCUMENT-IDENTIFIER: US 5830453 A

TITLE: Use of IL-13 to induce 15-lipoxygenase

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
------	-------	----------	-------	--------	----------------	------	-----------	--------	-----	-------

## 8. Document ID: US 5814517 A

Entry 8 of 14

File: USPT

Sep 29, 1998

US-PAT-NO: 5814517

DOCUMENT-IDENTIFIER: US 5814517 A

TITLE: DNA spacer regulatory elements responsive to cytokines and methods for their use

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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## 9. Document ID: US 5712094 A

Entry 9 of 14

File: USPT

Jan 27, 1998

US-PAT-NO: 5712094

DOCUMENT-IDENTIFIER: US 5712094 A

TITLE: Methods for detecting modulators of cytokine action

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Image
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## 10. Document ID: US 5710023 A

Entry 10 of 14

File: USPT

Jan 20, 1998

US-PAT-NO: 5710023  
DOCUMENT-IDENTIFIER: US 5710023 A  
TITLE: IL-13 cytokine receptor chain

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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11. Document ID: US 5614191 A

Entry 11 of 14

File: USPT

Mar 25, 1997

US-PAT-NO: 5614191  
DOCUMENT-IDENTIFIER: US 5614191 A  
TITLE: IL-13 receptor specific chimeric proteins and uses thereof

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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12. Document ID: US 5596072 A

Entry 12 of 14

File: USPT

Jan 21, 1997

US-PAT-NO: 5596072  
DOCUMENT-IDENTIFIER: US 5596072 A  
TITLE: Method of refolding human IL-13

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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13. Document ID: AU 9741640 A, WO 9808957 A1

Entry 13 of 14

File: DWPI

Mar 19, 1998

DERWENT-ACC-NO: 1998-179442  
DERWENT-WEEK: 199831  
COPYRIGHT 2000 DERWENT INFORMATION LTD  
TITLE: Chimeric molecules which bind to an interleukin-13 receptor - with blocker of interleukin-4 receptor, for delivery of effector molecules to tumours bearing IL-13 receptor

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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14. Document ID: JP 11511028 W, WO 9720926 A1, FR 2742156 A1, AU 9675760 A, ZA 9610238 A, NO 9802550 A, EP 876482 A1, BR 9611697 A

Entry 14 of 14

File: DWPI

Sep 28, 1999

DERWENT-ACC-NO: 1997-319773  
DERWENT-WEEK: 199952  
COPYRIGHT 2000 DERWENT INFORMATION LTD  
TITLE: New purified human interleukin-13 receptors - and related nucleic acids, useful for diagnosis and treatment of inflammation, allergy, etc

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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Term	Documents
IL-4	1637
IL-4S	10
RECEPTOR	70543
RECEPTORS	37269
IL4	323
IL4S	1
1 AND ((IL4 ADJ RECEPTOR) OR (IL-4 ADJ RECEPTOR))	14

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including document number

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Term	Documents
IL-4	1637
IL-4S	10
RECEPTOR	70543
RECEPTORS	37269
IL4	323
IL4S	1
1 AND ((IL4 ADJ RECEPTOR) OR (IL-4 ADJ RECEPTOR))	14

Database: [All Databases \(USPT + EPAB + JPAB + DWPI + TDBD\)](#)

11 and (il-4 receptor or il4 receptor)

Refine Search:

**Search History**

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
ALL	11 and (il-4 receptor or il4 receptor)	14	<a href="#">L3</a>
ALL	11 and il-4 receptor or il4 receptor	34	<a href="#">L2</a>
ALL	il-13 receptor or il13 receptor	23	<a href="#">L1</a>

\*\*\*\*\*STN Columbus\*\*\*\*\*  
..

FILE 'MEDLINE'  
FILE 'APIO'  
FILE 'BIOSIS'  
FILE 'SCISEARCH'  
FILE 'CAPLUS'  
FILE 'EMBASE'  
=> s haemopoietin receptor#

L1 19 HAEMOPOIETIN RECEPTOR#

=> s gcsf receptor# or g-csf receptor#

L2 1350 GCSF RECEPTOR# OR G-CSF RECEPTOR#

=> s il-13 receptor# or il3 receptor#

L3 357 IL-13 RECEPTOR# OR IL13 RECEPTOR#

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 108 DUP REM L3 (249 DUPLICATES REMOVED)

=> s l4 and (il4 or il-4)

L5 82 L4 AND (IL4 OR IL-4)

=> d l5 ibib abs 1-82

L5 ANSWER 1 OF 82 MEDLINE

ACCESSION NUMBER: 2000166405 MEDLINE

DOCUMENT NUMBER: 20166405

TITLE: Interleukin-4 and interleukin-13 act on glomerular visceral epithelial cells.

AUTHOR: Van Den Berg J G; Aten J; Chand M A; Claessen N; Dijkink L; Wijdenes J; Lakis F G; Weening J J  
CORPORATE SOURCE: Department of Pathology, Academic Medical Center, University of Amsterdam, The Netherlands.. j.g.vandenbergh@amc.uva.nl

SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (2000 Mar) 11 (3) 413-22.

Journal code: A6H. ISSN: 1046-6673.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200005

ENTRY WEEK: 20000504

AB In minimal change nephrosis (MCN), proteinuria is associated with structural changes of the glomerular visceral epithelial cells (GVEC). The occurrence of MCN has been associated with 2 lymphocyte-dependent conditions. To examine a direct role for type 2 cytokines in GVEC injury, the expression of interleukin ( \*\*\*IL\*\*\* ) - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* and IL-13 on GVEC were studied. Reverse transcription-PCR showed that isolated human and rat glomeruli and cultured human and rat GVEC expressed mRNA for IL-4Ralpha, IL-13Ralpha1, and IL-13Ralpha2. Protein expression of IL-4Ralpha and IL-13Ralpha2 by GVEC in human kidney biopsies and by cultured human GVEC was detected by immunohistochemistry. Western blotting demonstrated phosphorylation of STAT6 in cultured GVEC upon incubation with \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13. This indicated signal transduction via the heterodimeric receptor complex IL-4R2, which is composed of the IL-4Ralpha and the IL-13Ralpha1. Direct effects on GVEC function were examined in monolayer experiments. \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 dose-dependently decreased transepithelial electrical resistance of monolayers of rat GVEC to approximately 30 and 40% of baseline values, respectively. The transepithelial electrical resistance decrease was associated with a significant increase in short-circuit current, whereas no changes were observed in the transmonolayer flux of the macromolecules horseradish peroxidase (molecular weight, 44 kD) and

14C-mannitol (molecular weight, 182 Da). No changes in cell structure were observed with electron microscopy. It is concluded that by binding to specific \*\*\*IL\*\*\* - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\*, \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 can exert specific effects on GVEC function, which could be of pathogenetic relevance for glomerular injury in MCN.

L5 ANSWER 2 OF 82 MEDLINE

ACCESSION NUMBER: 2000106191 MEDLINE

DOCUMENT NUMBER: 20106191

TITLE: Sharing of receptor subunits and signal transduction pathway between the \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* system.

AUTHOR: Murata T; Taguchi J; Puri R K; Mohri H  
CORPORATE SOURCE: First Department of Internal Medicine, School of Medicine, Yokohama City University, Japan.

SOURCE: INTERNATIONAL JOURNAL OF HEMATOLOGY, (1999 Jan) 69 (1) 13-20. Ref: 56

Journal code: A7F. ISSN: 0925-5710.

PUB. COUNTRY: Ireland

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW) (REVIEW, TUTORIAL)

LANGUAGE: English

ENTRY MONTH: 200004

ENTRY WEEK: 20000403

AB In this review, we summarize the subunit structure of the interleukin ( \*\*\*IL\*\*\* ) - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* system and the molecular mechanism of signals through the cytokine receptor systems. We have demonstrated that two different forms of IL-4R exist, classical and alternative. Classical IL-4R is predominantly expressed in hematopoietic cells and consists of IL-4R p140 (beta) and IL-2R gamma (gamma c) chains. The alternative form of IL-4R is predominantly expressed in nonhematopoietic cells and consists of IL-4R beta and IL-13R alpha' chains. Moreover, the alternative form of IL-4R is also used as a functional component in the IL-13R complex. For signal transduction through IL-4R and IL-13R, we have demonstrated that in nonhematopoietic cells, Janus protein tyrosine kinase (JAK) 2 is phosphorylated and activated instead of JAK3 tyrosine kinase. While JAK3 is required for signal transducer and activator of transcription-6 (STAT6) activation in hematopoietic cells, we recently demonstrated that in nonhematopoietic cells JAK2 is required for STAT6 activation for the alternative form of IL-4R. Thus, a major difference exists between hematopoietic and nonhematopoietic cells with regard to structure and signal transduction through the IL-4R and IL-13R systems.

L5 ANSWER 3 OF 82 MEDLINE  
ACCESSION NUMBER: 2000079111 MEDLINE  
DOCUMENT NUMBER: 20079111  
TITLE: Binding of \*\*\*IL\*\*\* - \*\*\*4\*\*\* to the IL-13Ralpha1/IL-4Ralpha receptor complex leads to STAT3 phosphorylation but not to its nuclear translocation.  
AUTHOR: Wery-Zennaro S; Letoumeur M; David M; Bertoglio J; Pierre J  
CORPORATE SOURCE: INSERM U461, Faculte de Pharmacie, 5, rue J.B. Clement, 92296, Chatenay-Malabry, France.  
SOURCE: FEBS LETTERS, (1999 Dec 24) 464 (1-2) 91-6. Journal code: EUH. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 200003  
ENTRY WEEK: 20000305  
AB Interleukin-4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) is a pleiotropic cytokine, which acts on both hematopoietic and non-hematopoietic cells,

through different types of receptor complexes. In this study, we report that in human B cells, \*\*\*IL\*\*\* - \*\*\*4\*\*\* caused rapid phosphorylation of Janus kinase (JAK) 1 and JAK3 tyrosine kinases. In keratinocytes, the hematopoietic-specific receptor common gamma(c) chain is not expressed and the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* alpha(1) (IL-13Ralpha(1)) participates in \*\*\*IL\*\*\* - \*\*\*4\*\*\* signal transduction. In keratinocytes, \*\*\*IL\*\*\* - \*\*\*4\*\*\* induced JAK1 and JAK2 phosphorylation but, unlike in immune cells, \*\*\*IL\*\*\* - \*\*\*4\*\*\* did not involve JAK3 activation for its signaling. In both cell types, \*\*\*IL\*\*\* - \*\*\*4\*\*\* induced phosphorylation and DNA binding activation of the signal transducer and activator of transcription (STAT) 6 protein. Furthermore, \*\*\*IL\*\*\* - \*\*\*4\*\*\* stimulation of keratinocytes also induced tyrosine phosphorylation of STAT3 which was found to bind to the phosphorylated IL-13Ralpha(1). STAT3 however did not significantly translocate to the nucleus, nor did it bind with high affinity to target DNA sequences.

L5 ANSWER 4 OF 82 MEDLINE

ACCESSION NUMBER: 2000001678 MEDLINE

DOCUMENT NUMBER: 20001678

TITLE: Differential responses of human monocytes and macrophages to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13.

AUTHOR: Hart P H; Bonder C S; Balogh J; Dickensheets H L; Donnelly R P; Finlay-Jones J J

CORPORATE SOURCE: Department of Microbiology & Infectious Diseases, School of Medicine, Flinders University of South Australia, Adelaide, Australia.

SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1999 Oct) 66 (4) 575-8. Ref: 39

Journal code: IWY. ISSN: 0741-5400.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW) (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 200001

ENTRY WEEK: 20000104

AB The primary interleukin-4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) receptor complex on monocytes (type I \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor) includes the 140-kDa alpha chain (IL-4R alpha) and the IL-2 receptor gamma chain, gamma(c), which heterodimerize for intracellular signaling, resulting in suppression of lipopolysaccharide (LPS)-inducible inflammatory mediator production. The activity of IL-13 on human monocytes is very similar to that of \*\*\*IL\*\*\* - \*\*\*4\*\*\* because the predominant signaling chain (IL-4R alpha) is common to both receptors. In fact, IL-4R alpha with IL-13R alpha1 is designated both as an \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* and the type II \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor. When the anti-inflammatory activities of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 were investigated on synovial fluid macrophages and compared with the responses by monocytes isolated from the patients at the same time as joint drainage, the response profiles differed with some responses similar in the two cell populations, others reduced on the inflammatory cells. Similar differences were recorded in the response profiles to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 by monocytes and monocytes cultured for 7 days in macrophage colony-stimulating factor (M-CSF) or granulocyte-macrophage CSF (GM-CSF) (monocyte-derived macrophages, MDMac). MDMac have reduced gamma(c) mRNA levels and reduced expression of the functional 64-kDa gamma(c). There was a similar loss of IL-13R alpha1 mRNA on monocyte

differentiation. In turn, there was a significant reduction in the ability of \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13 to activate STAT6. These findings suggest that different functional responses to \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13 by human monocytes and macrophages may result from reduced expression of gamma(c) and IL-13R alpha1.

L5 ANSWER 5 OF 82 MEDLINE  
ACCESSION NUMBER: 1999445551 MEDLINE  
DOCUMENT NUMBER: 99445551  
TITLE: Mutants of interleukin 13 with altered reactivity toward interleukin 13 receptors.  
AUTHOR: Thompson J P; Debinski W  
CORPORATE SOURCE: Section of Neurosurgery/H110, Department of Surgery, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033-0850, USA.  
CONTRACT NUMBER: CA 74145 (NCI)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 15) 274 (42) 29944-50.  
Journal code: HIV. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 200001  
ENTRY WEEK: 20000104  
AB Interleukin 13 (IL13) belongs to a family of cytokines whose members exhibit structural homology, despite amino acid sequence dissimilarity.  
For example, while of limited sequence homology, IL13 and \*\*\*IL4\*\*\* share a signaling receptor, IL13/4 receptor, on a variety of human normal cells. However, a subclass of \*\*\*IL4\*\*\* -independent \*\*\*IL13\*\*\* receptors is overexpressed on certain transformed cells, including human malignant gliomas. We introduced mutations into human (h) IL13 to determine the site(s) involved in interaction with the shared receptor and/or the glioma-associated receptor. This analysis identified at least three protein regions that are needed for signaling through the shared receptor. These regions were localized to alpha-helices A, C, and D and were mainly separate from the region(s) needed to interact with the glioma-associated receptor. Glutamic acids at positions 13 and 16 in hIL13 alpha-helix A, arginine and serine at positions 66 and 69 in helix C, and arginine at position 109 in helix D were found to be important in inducing biological signaling since their specific mutation resulted in loss and/or gain of function phenomena. We demonstrate that the molecular requirements of hIL13 to interact with its respective receptors are generally distinct and can be controlled by mutagenesis of the cytokine.

L5 ANSWER 6 OF 82 MEDLINE  
ACCESSION NUMBER: 1999288091 MEDLINE  
DOCUMENT NUMBER: 99288091  
TITLE: Differences between \*\*\*IL\*\*\* . \*\*\*4\*\*\* and \*\*\*IL\*\*\* . \*\*\*4\*\*\* receptor alpha-deficient mice in chronic leishmaniasis reveal a protective role for \*\*\*IL\*\*\* . \*\*\*13\*\*\* receptor signaling.  
AUTHOR: Mohr M; Ledermann B; Kohler G; Dorfmueller A; Gessner A; Brombacher F  
CORPORATE SOURCE: Max-Planck-Institute for Immunobiology, Freiburg, Germany.  
SOURCE: JOURNAL OF IMMUNOLOGY, (1999 Jun 15) 162 (12) 7302-8.  
Journal code: IFB. ISSN: 0022-1767.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
ENTRY MONTH: 199909  
ENTRY WEEK: 19990901  
AB \*\*\*IL\*\*\* . \*\*\*4\*\*\* receptor alpha-chain-deficient (IL-4Ralpha-/-) mice were generated by homologous and site-specific

recombination, using the Cre/loxP system in BALB/c-derived embryonic stem cells. In vitro analysis of cells from these mice revealed impaired \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13-mediated functions, demonstrating that the IL-4Ralpha-chain is an essential component of both the \*\*\*IL\*\*\* . \*\*\*4\*\*\* and the \*\*\*IL\*\*\* . \*\*\*13\*\*\* receptor. Whereas Leishmania major-infected BALB/c mice developed fatal progressive disease with type 2 Ab responses within 3 mo, both IL-4Ralpha-/- and \*\*\*IL\*\*\* . \*\*\*4\*\*\* -/- BALB/c mice contained infection with reduced footpad swelling, parasite load, moderate histopathology, and type 1 Ab responses during this time period. Conclusively, these results demonstrate an \*\*\*IL\*\*\* . \*\*\*4\*\*\* -dependent mechanism of susceptibility in BALB/c mice. Nevertheless, in contrast to mutant mice, infected C57BL/6 mice healed completely within 3 mo, indicating that additional factors are necessary for subsequent healing and elimination of the pathogen. During the further course of infection, IL-4Ralpha-/- mice developed progressive disease with massive footpad swelling. Lesions became ulcerative and necrotic with subsequent destruction of connective tissue and bones, as well as dissemination into organs and consequent mortality within the monitored 6 mo of chronic infection. In striking contrast, \*\*\*IL\*\*\* . \*\*\*4\*\*\* -/- mice maintained control of infection on a moderate level, but were unable to clear the pathogen. The distinct phenotypes of the BALB/c embryonic stem cell-derived \*\*\*IL\*\*\* . \*\*\*4\*\*\* -/- and IL-4Ralpha-/- mouse strains identify previously unsuspected mechanisms for maintaining host immunity to chronic infection with L. major, mediated by a functional \*\*\*IL\*\*\* . \*\*\*13\*\*\* receptor.

L5 ANSWER 7 OF 82 MEDLINE  
ACCESSION NUMBER: 1999280197 MEDLINE  
DOCUMENT NUMBER: 99280197  
TITLE: Receptor for interleukin 13 is a marker and therapeutic target for human high-grade gliomas.  
AUTHOR: Debinski W; Gibo D M; Hulet S W; Connor J R; Gillespie G Y  
CORPORATE SOURCE: Department of Surgery, Pennsylvania State University College of Medicine, Hershey 17033-0850, USA.. wdebinski@psghs.edu  
CONTRACT NUMBER: R01 CA74145 (NCI)  
SOURCE: CLINICAL CANCER RESEARCH, (1999 May) 5 (5) 985-90.  
Journal code: C2H. ISSN: 1078-0432.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199910  
ENTRY WEEK: 19991001  
AB Glioblastoma multiforme (GBM) is an incurable brain tumor. Due to the striking heterogeneity that characterizes GBM, there is no known tumor-specific antigen or receptor that is expressed by a majority of GBM patients. We found that virtually all studied human GBM specimens (23 samples) abundantly expressed a receptor for interleukin (IL)-13 in situ, whereas normal human brain had few, if any, IL-13-binding sites. The GBM-associated \*\*\*IL\*\*\* . \*\*\*13\*\*\* receptor was both quantitatively and qualitatively different from and, thus, more restrictive than the shared signaling receptor of normal tissue: it was \*\*\*IL\*\*\* . \*\*\*4\*\*\* independent. The receptor for IL-13 was overexpressed by a majority of cancer cells in situ. Furthermore, cytotoxins targeted to this more restrictive IL-13R produced cures in animals bearing xenografts of human high-grade gliomas. Thus, unexpectedly, the receptor for an immune regulatory

cytokine may be a long sought marker and, concomitantly, a unique imaging site and therapeutic target for GBM, the most malignant and the most heterogeneous of brain tumors.

L5 ANSWER 8 OF 82 MEDLINE  
ACCESSION NUMBER: 1999243120 MEDLINE  
DOCUMENT NUMBER: 99243120  
TITLE: Pancreatic cancer cells express interleukin-13 and -4 receptors, and their growth is inhibited by Pseudomonas exotoxin coupled to interleukin-13 and -4.  
AUTHOR: Kornmann M; Kleeff J; Debinski W; Kore M  
CORPORATE SOURCE: Department of Medicine, University of California, Irvine 92697, USA. mkore@uci.edu  
CONTRACT NUMBER: CA-40162 (NCI)  
SOURCE: ANTICANCER RESEARCH, (1999 Jan-Feb) 19 (1A) 125-31.  
Journal code: 59L. ISSN: 0250-7005.  
PUB. COUNTRY: Greece  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199907  
ENTRY WEEK: 19990704  
AB BACKGROUND: Interleukin (IL)-13 and -4 are multifunctional cytokines that bind to specific cell-surface receptors. The aim of this study was to determine whether pancreatic cancer cells express either receptor, and to assess the growth suppressive effects of chimeric proteins composed of a Pseudomonas exotoxin (PE) A mutant (PE38QQR) fused to IL-13 (IL-13-PE38QQR) or \*\*\*IL\*\*\* . \*\*\*4\*\*\* (\*\*\*IL\*\*\* . \*\*\*4\*\*\*-PE38QQR) in these cells. MATERIALS AND METHODS: Northern and Western blot analysis were used to analyze the expression of \*\*\*IL\*\*\* . \*\*\*4\*\*\* -13 receptors and the common gamma chain (gamma c) in pancreatic cancer cell lines. MTT growth assays were carried out to assess the effects of \*\*\*IL\*\*\* . \*\*\*4\*\*\* -13 and \*\*\*IL\*\*\* . \*\*\*4\*\*\* -13-PE38QQR on cell growth. RESULTS: All 6 pancreatic cancer cell lines examined expressed IL-13R alpha 1 and IL-4R alpha, one cell line expressed IL-13R alpha 2, and 5 pancreatic cancer cell lines expressed gamma c. IL-13 (5 nM) significantly enhanced the growth of 3 cell lines, whereas \*\*\*IL\*\*\* . \*\*\*4\*\*\* (5 nM) enhanced the growth of 1 cell line. In contrast, IL-13-PE38QQR and \*\*\*IL\*\*\* . \*\*\*4\*\*\*-PE38QQR inhibited the growth of all 6 tested cell lines. There were large variations in the individual sensitivity of the cells, with LD50 values ranging from 100 ng/ml to 5 micrograms/ml for IL-13-PE38QQR and from 20 ng/ml to 10 micrograms/ml for \*\*\*IL\*\*\* . \*\*\*4\*\*\*-PE38QQR. IL-13 and -4 antagonized these inhibitory activities in some, but not all, of the cell lines. CONCLUSIONS: IL-13 and -4 may act as mitogens toward pancreatic cancer cells by activating \*\*\*IL\*\*\* . \*\*\*4\*\*\* - and \*\*\*IL\*\*\* . \*\*\*13\*\*\* receptors and IL-13 and \*\*\*IL\*\*\* . \*\*\*4\*\*\* -coupled toxins may ultimately have a role in the treatment of pancreatic cancer.

L5 ANSWER 9 OF 82 MEDLINE  
ACCESSION NUMBER: 1999215813 MEDLINE  
DOCUMENT NUMBER: 99215813  
TITLE: An immune regulatory cytokine receptor and glioblastoma multiforme: an unexpected link.  
AUTHOR: Debinski W  
CORPORATE SOURCE: Department of Surgery, Pennsylvania State University College of Medicine, Hershey 17033-0850, USA.  
SOURCE: CRITICAL REVIEWS IN ONCOGENESIS, (1998) 9 (3-4) 253-68.  
Ref: 81  
Journal code: A1Y. ISSN: 0893-9675.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199906  
 ENTRY WEEK: 19990604  
 AB Human high-grade gliomas (HGG) are one of the most devastating human malignancies. They are rapidly progressing heterogenous tumors for which no curable treatment is available. Although these tumors are believed to be of glial cell origin, known tumor-specific markers do not characterize them. The specific environmental conditions that cause or promote the development of HGG are not known. The pathomechanism of HGG is yet to be revealed, although more specific genetic alterations are assigned to HGG. Recently, we have found that HGG overexpress a receptor for an immune regulatory cytokine, interleukin-13 (IL-13). In fact, it appears that all patients with glioblastoma multiforme may possess this receptor. IL-13 is an antiinflammatory cytokine with many overlapping functions to its homologue, \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*. There is a high degree of specificity of the overexpression of the \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptor\*\*\* in HGG. This receptor is not only quantitatively but also qualitatively different from the only known functional signaling receptor for IL-13 of normal tissue. It is not shared with \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*. The more restrictive receptor for IL-13 thus may represent a new factor specific for a disease as heterogenous as HGG.

L5 ANSWER 10 OF 82 MEDLINE  
 ACCESSION NUMBER: 1999171151 MEDLINE  
 DOCUMENT NUMBER: 99171151  
 TITLE: Binding of interleukin-13 and interleukin-4 to the

interleukin ( \*\*\*IL\*\*\* ). \*\*\*\*4\*\*\* / \*\*\*IL\*\*\*  
 -  
 \*\*\*13\*\*\* \*\*\*receptor\*\*\* of human synovial fibroblasts.

AUTHOR: Lutz R A; Feng N; Moser R  
 CORPORATE SOURCE: Institute of Clinical Chemistry, University Hospital, Zurich.

SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (1999 Jan-Jul) 19 (1-4) 181-90.  
 Journal code: CCU. ISSN: 1079-9893.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199908  
 ENTRY WEEK: 19990803

AB Synovial fibroblasts expressed transcripts for IL-4R alpha, and IL-13R

alpha 1 and IL-13R alpha 2. Using weighted nonlinear computer modeling of the data from equilibrium binding studies, a 2 bindings sites model fitted the data best. After occupation of the shared high affinity receptors by the non-signaling, double mutant \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* (121)R-->D, 124Y-->D (RY: \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* ) the high affinity binding of IL-13

could be abolished. A 2 binding site model still could be fitted, however the improvement in fit over a onesite model was not statistically significant. Using affinity spectra, at least 2 binding sites are apparent. After treatment with RY: \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* , some of the high affinity binding was abolished, however not completely. A correlation between the number of binding sites and the affinity is apparent, which seriously casts doubt on the classical evaluation of binding isotherms, where the parameters are assumed to be independent. In a previous study we suggested that the large number of IL-13R alpha 2 monomers are silent receptors, likely representing a decoy target for IL-13. The high affinity binding therefore most likely represents the binding to the heterodimer consisting of IL-4R alpha and IL-13R alpha 1 or IL-13R alpha 2. The low affinity binding may represent the IL-13R alpha 2.

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SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (1999 Jan-Jul) 19 (1-4) 181-90.  
 Journal code: CCU. ISSN: 1079-9893.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
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 ENTRY WEEK: 19990803

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 -  
 \*\*\*13\*\*\* \*\*\*receptor\*\*\* of human synovial fibroblasts.

L5 ANSWER 11 OF 82 MEDLINE  
 ACCESSION NUMBER: 1999113371 MEDLINE  
 DOCUMENT NUMBER: 99113371  
 TITLE: Interleukin-4 and interleukin-13: their similarities and discrepancies.

AUTHOR: Chomarat P; Banchereau J  
 CORPORATE SOURCE: Schering-Plough, Laboratory for Immunological Research, Dardilly, France.

SOURCE: INTERNATIONAL REVIEWS OF IMMUNOLOGY, (1998) 17 (1-4) 1-52.

Ref: 300  
 Journal code: IRI. ISSN: 0883-0185.

PUB. COUNTRY: Switzerland  
 Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199906  
 ENTRY WEEK: 19990601

AB Interleukin-4 ( \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* ) and the closely related cytokine, interleukin-13 (IL-13) share many biological and immunoregulatory functions on B lymphocytes, monocytes, dendritic cells and fibroblasts.

Both \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 genes are located in the same vicinity on chromosome 5 and display identical major regulatory sequences in their respective promoters, thus explaining their restricted secretion pattern to activated T cells and mast cells. The \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptors\*\*\* are multimeric and share at least one common chain called IL-4R alpha. Recent progress made in the description of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*\*13\*\*\*

\*\*\*receptor\*\*\* complex have demonstrated the existence of two types of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptors: one constituted by the IL-4R alpha and the gamma c chain, and a second constituted by the \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* R alpha and the IL-13R alpha 1 and able to transduce both \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 signals. Specific \*\*\*IL\*\*\* - \*\*\*\*13\*\*\*

\*\*\*receptors\*\*\* are results from the association between the IL-4R alpha and the IL-13R alpha 2 or between two IL-13R alpha. Furthermore, similarities in \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 signal transduction have been also described, thus explaining the striking overlapping of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* - and IL-13-induced biological activities such as regulation of antibody production and inflammation.

However, the restricted expression of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* to type 2 helper T lymphocytes as well as the inability of IL-13 to regulate T cell differentiation due to a lack of \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptors\*\*\* on T lymphocytes represent the major differences between these cytokines. This would indicate that although \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 share a large number of properties, precise mechanisms of regulation are also present to guarantee their distinct functions.

L5 ANSWER 12 OF 82 MEDLINE  
 ACCESSION NUMBER: 1999077182 MEDLINE  
 DOCUMENT NUMBER: 99077182

TITLE: The distribution of \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptor\*\*\* alpha 1 expression on B cells, T cells and monocytes and its regulation by IL-13 and \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*

AUTHOR: Graber P; Gretener D; Herren S; Aubry J P; Elson G; Poudrier J; Lecoanet-Henchoz S; Alouani S; Losberger C; Bonnefoy J Y; Kosco-Vilbois M H; Gauchat J F

CORPORATE SOURCE: Geneva Biomedical Research Institute, Plan-les-Ouates, Switzerland.

SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1998 Dec) 28 (12) 4286-98.  
 Journal code: EN5. ISSN: 0014-2980.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199903  
 ENTRY WEEK: 19990301

AB To study the expression of \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptor\*\*\* alpha 1 (IL-13Ralpha1), specific monoclonal antibodies (mAb) were generated. Surface expression of the IL-13Ralpha1 on B cells, monocytes and T cells was assessed by flow cytometry using these specific mAb. Among tonsillar B cells, the expression was the highest on the IgD+ CD38- B cell subpopulation which is believed to represent naive B cells. Expression was also detectable on a large fraction of the IgD-CD38- B cells but not on CD38+ B cells. Activation under conditions which promote B cell Ig class switching up-regulated the expression of the receptor. However, the same stimuli had an opposite effect for IL-13Ralpha1 expression levels on monocytes. While IL-13Ralpha1 mRNA was clearly detectable in T cell preparations, no surface expression was detected. However, permeabilization of the T cells showed a clear intracellular expression of the receptor. A soluble form of the receptor was immunoprecipitated from the supernatant of activated peripheral T cells, suggesting that T cell IL-13Ralpha1 might have functions unrelated to the capacity to form a type II \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* /IL-13R with IL-4Ralpha.

L5 ANSWER 13 OF 82 MEDLINE  
 ACCESSION NUMBER: 1999034937 MEDLINE  
 DOCUMENT NUMBER: 99034937

TITLE: Human glioma cells overexpress receptors for interleukin 13 and are extremely sensitive to a novel chimeric protein composed of interleukin 13 and pseudomonas exotoxin.

AUTHOR: Debinski W; Obiri N I; Powers S K; Pastan I; Puri R K  
 CORPORATE SOURCE: The Milton S. Hershey Medical Center, The Pennsylvania State University College of Medicine, Department of Surgery, Division of Neurosurgery, Hershey, Pennsylvania 17033, USA.. debinski@debin.nsr.hmc.psu.edu

SOURCE: CLINICAL CANCER RESEARCH, (1995 Nov) 1 (11) 1253-8.  
 Journal code: C2H. ISSN: 1078-0432.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
 ENTRY WEEK: 19990402

AB Recently, we have demonstrated that a spectrum of human adenocarcinoma cell lines express binding sites for interleukin 13 (IL-13). These cells are killed by a chimeric protein composed of human (h) IL-13 and a derivative of Pseudomonas exotoxin, PE38QQR (Debinski et al, J. Biol. Chem., 270: 16775-16780, 1995). The cell killing was hIL-13- and hIL-4-specific, indicating that a common binding site for the two cytokines is present in several solid tumor cell lines. Herein, we report that an array of established glioma cell lines is killed by very low concentrations of hIL-13-PE38QQR, often reaching <1 ng/ml (<20 pM). Glioma cells express up to 30,000 molecules of \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptor\*\*\* /cell which has intermediate affinity toward hIL-13. hIL-13-PE38QQR is more active (up to 3 logs difference in cytotoxic activities) than are the corresponding chimeric toxins containing hIL-4 or hIL-6. The cytotoxic action of hIL-13-PE38QQR is blocked by an excess of hIL-13 on all cell lines studied, and it is not neutralized by hIL-4 on some of these cells. Our results show that human brain cancers richly express receptors for IL-13. Furthermore, the interaction detected previously between receptors for IL-13 and \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*

Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199903  
 ENTRY WEEK: 19990301

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L5 ANSWER 13 OF 82 MEDLINE  
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SOURCE: CLINICAL CANCER RESEARCH, (1995 Nov) 1 (11) 1253-8.  
 Journal code: C2H. ISSN: 1078-0432.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
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Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
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L5 ANSWER 13 OF 82 MEDLINE  
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SOURCE: CLINICAL CANCER RESEARCH, (1995 Nov) 1 (11) 1253-8.  
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PUB. COUNTRY: United States  
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LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
 ENTRY WEEK: 19990402

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Journal; Article; (JOURNAL ARTICLE)  
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L5 ANSWER 13 OF 82 MEDLINE  
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SOURCE: CLINICAL CANCER RESEARCH, (1995 Nov) 1 (11) 1253-8.  
 Journal code: C2H. ISSN: 1078-0432.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
 ENTRY WEEK: 19990402

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 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
 ENTRY WEEK: 19990402

AB Recently, we have demonstrated that a spectrum of human adenocarcinoma cell lines express binding sites for interleukin 13 (IL-13). These cells are killed by a chimeric protein composed of human (h) IL-13 and a derivative of Pseudomonas exotoxin, PE38QQR (Debinski et al, J. Biol. Chem., 270: 16775-16780, 1995). The cell killing was hIL-13- and hIL-4-specific, indicating that a common binding site for the two cytokines is present in several solid tumor cell lines. Herein, we report that an array of established glioma cell lines is killed by very low concentrations of hIL-13-PE38QQR, often reaching <1 ng/ml (<20 pM). Glioma cells express up to 30,000 molecules of \*\*\*IL\*\*\* - \*\*\*\*13\*\*\* \*\*\*receptor\*\*\* /cell which has intermediate affinity toward hIL-13. hIL-13-PE38QQR is more active (up to 3 logs difference in cytotoxic activities) than are the corresponding chimeric toxins containing hIL-4 or hIL-6. The cytotoxic action of hIL-13-PE38QQR is blocked by an excess of hIL-13 on all cell lines studied, and it is not neutralized by hIL-4 on some of these cells. Our results show that human brain cancers richly express receptors for IL-13. Furthermore, the interaction detected previously between receptors for IL-13 and \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*

Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
 ENTRY WEEK: 19990402

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Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
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 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199904  
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\*\*\*4\*\*\* on solid tumors cell lines is of a qualitatively different character in U-251 MG and U-373 MG glioma cells. The receptor for IL-13 may represent a new marker of brain cancers and an attractive target for anticancer therapies.

L5 ANSWER 14 OF 82 MEDLINE  
ACCESSION NUMBER: 1998391042 MEDLINE  
DOCUMENT NUMBER: 98391042  
TITLE: The murine \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
\*\*\*receptor\*\*\*

alpha 2: molecular cloning, characterization, and comparison with murine \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
\*\*\*receptor\*\*\* alpha 1.

AUTHOR: Donaldson D D; Whitters M J; Fitz L J; Neben T Y; Finnerty H; Henderson S L; O'Hara R M Jr; Beier D R; Turner K J;

Wood C R; Collins M  
CORPORATE SOURCE: Genetics Institute, Immunology Department, Cambridge, MA 02140, USA.

CONTRACT NUMBER: RO1 HD29028 (NICHHD)  
RO1HG00951 (NHGRJ)  
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Sep 1) 161 (5) 2317-24.

Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

OTHER SOURCE: GENBANK-U65747  
ENTRY MONTH: 199811

AB Two components of a receptor complex for IL-13, the IL-4R and a low affinity IL-13-binding chain, IL-13R alpha 1, have been cloned in mice and humans. An additional high affinity binding chain for IL-13, IL-13R alpha

2, has been described in humans. We isolated a cDNA from the thymus that encodes the murine orthologue of the human IL-13R alpha

2. The predicted protein sequence of murine IL-13R alpha 2 (mIL-13R alpha 2) has 59% overall identity to human IL-13R alpha 2 and is closely related to the murine low affinity IL-13-binding subunit, IL-13R alpha 1.

The genes for both mIL-13-binding chains map to the X chromosome. A specific interaction between mIL-13R alpha 2Fc protein and IL-13 was demonstrated by surface plasmon resonance using a BIACORE instrument. Ba/F3 cells that were transfected with mIL-13R alpha 2 expressed 5000 molecules per cell and bound IL-13 with a single Kd of 0.5 to 1.2 nM. However, these cells did not proliferate in response to IL-13, and the \*\*\*IL\*\*\* - \*\*\*4\*\*\*

dose response was unaffected by high concentrations of IL-13. In contrast, the expression of mIL-13R alpha 1 by Ba/F3 cells resulted in a sensitive proliferative response to IL-13. Consistent with its lower affinity for IL-13, IL-13R alpha 1Fc was 100-fold less effective than IL-13R alpha

2Fc in neutralizing IL-13 in vitro. These results show that mIL-13R alpha 2 and mIL-13R alpha 1 are not functionally equivalent and predict distinct roles for each polypeptide in IL-13R complex formation and in the modulation of IL-13 signal transduction.

L5 ANSWER 15 OF 82 MEDLINE  
ACCESSION NUMBER: 1998389089 MEDLINE  
DOCUMENT NUMBER: 98389089  
TITLE: Two different \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
\*\*\*receptor\*\*\* chains are expressed in normal human skin fibroblasts, and \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 mediate signal transduction through a common pathway.

AUTHOR: Murata T; Husain S R; Mohri H; Puri R K  
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapy, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD 20892, USA.

SOURCE: INTERNATIONAL IMMUNOLOGY, (1998 Aug 10 (8)) 1103-10.

Journal code: AY5. ISSN: 0953-8178.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199901  
ENTRY WEEK: 19990104  
AB IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\*, pleiotropic immune regulatory cytokines, have been shown to mediate similar prominent effects in human fibroblast cell lines. However, molecular mechanisms for their redundant effects are not known. Here, we have investigated the structure of \*\*\*IL\*\*\* - \*\*\*13\*\*\* -receptors\*\*\* (IL-13R) and molecular mechanisms of signal transduction through IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptors in non-transformed normal skin fibroblast cell lines. We demonstrate that high-affinity IL-13R is expressed in normal skin fibroblast cell lines. Upon [125I]IL-13 cross-linking, a approximately 60-70 kDa band was observed in sk559 and sk574 fibroblast cell lines. By RT-PCR analysis, mRNA for IL-13R alpha, IL-13R alpha' and IL-4Rbeta chains were expressed; however, the IL-2Rgamma chain, shown to participate and modulate \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 binding, was not expressed in any of the cell lines examined. The Janus kinase (JAK)2 and Tyk2 were phosphorylated in response to \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13 in sk559 and sk574 cell lines. JAK1 was also phosphorylated in one of two cell lines while JAK3 was present but not phosphorylated in any of the cell lines studied. A signal transduction and activator of transcription (STAT)6 was also activated in response to both IL. An insulin receptor substrate (IRS)-1 was constitutively phosphorylated and its phosphorylation level was augmented in response to both IL. These results suggest that the mechanism of signal transduction through IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptors in human fibroblast cell lines is similar, and this may, at least in part, be responsible for the redundant effects of these two cytokines. In addition, JAK2 tyrosine kinase instead of JAK3 appears to play a major role in \*\*\*IL\*\*\* - \*\*\*4\*\*\* - and IL-13-induced signal transduction in human fibroblasts.

L5 ANSWER 16 OF 82 MEDLINE  
ACCESSION NUMBER: 1998389048 MEDLINE  
DOCUMENT NUMBER: 98389048  
TITLE: The role of IL-13 and its receptor in allergy and inflammatory responses.

AUTHOR: de Vries J E  
CORPORATE SOURCE: Novartis Research Institute, Vienna, Austria.  
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Aug) 102 (2) 165-9. Ref: 19  
Journal code: H53. ISSN: 0091-6749.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199812  
ENTRY WEEK: 19981201  
AB IL-13 is a cytokine that is produced by different T-cell subsets and dendritic cells. IL-13 shares many biologic activities with \*\*\*IL\*\*\* - \*\*\*4\*\*\*. This is due to the fact that IL-13- and \*\*\*IL\*\*\* - \*\*\*4\*\*\* -receptor complexes share the \*\*\*IL\*\*\* - \*\*\*4\*\*\* -receptor alpha-chain, which is important for signal transduction. T cells do not express functional \*\*\*IL\*\*\* - \*\*\*13\*\*\* -receptors\*\*\*. This is the reason why IL-13, in contrast to \*\*\*IL\*\*\* - \*\*\*4\*\*\*, fails to induce TH2-cell differentiation, one of the hallmarks of the allergic response. However, IL-13 is required for optimal induction of IgE synthesis, particularly in situations in which \*\*\*IL\*\*\* -

\*\*\*4\*\*\* production is low or absent. On the other hand, IL-13 inhibits proinflammatory cytokine and chemokine production in vitro and has potent antiinflammatory activities in vivo. From these observations, it can be concluded that IL-13 is an antiinflammatory cytokine that plays a unique role in the induction and maintenance of IgE production and IgE-mediated allergic responses.

L5 ANSWER 17 OF 82 MEDLINE  
ACCESSION NUMBER: 1998266220 MEDLINE  
DOCUMENT NUMBER: 98266220  
TITLE: The interleukin-4/interleukin-13 receptor of human synovial fibroblasts: overexpression of the nonsignaling interleukin-13 receptor alpha2.

AUTHOR: Feng N; Lugh S M; Schnyder B; Gauchat J F; Graber P; Schlagenhauf E; Schnarr B; Wiederkehr-Adam M; Duschl A;

Heim M H; Lutz R A; Moser R  
CORPORATE SOURCE: Institute of Clinical Chemistry, University Hospital, Zurich, Switzerland.

SOURCE: LABORATORY INVESTIGATION, (1998 May) 78 (5) 591-602.  
Journal code: KZA. ISSN: 0023-6837.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199808  
ENTRY WEEK: 19980804  
AB Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 are known to bind to shared heteromultimeric receptor complexes of variable composition. Given the many regulatory effects of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 on synovial cells, we aimed to characterize their \*\*\*IL\*\*\* - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* -receptor\*\*\* (R). Cultivated synovial fibroblasts expressed transcripts for IL-4Ralpha and IL-13Ralpha1, the human homolog of the recently cloned mouse IL-13R, but not the common gamma-chain of the IL-2R. In particular, IL-13Ralpha2 mRNA, encoding a different IL-13R recently cloned from human renal carcinoma cells, was expressed at a strikingly high level. Correspondingly, a predominant protein migrating at 65 to 75 kd was cross-linked by iodinated IL-13 and was not cross-competed by an excess of unlabeled \*\*\*IL\*\*\* - \*\*\*4\*\*\*. However, by flow cytometry, IL-13Ralpha1 (detected by the anti-IL-13Ralpha1 mAb 65) and IL-4Ralpha (detected by the mAb S697) were expressed at similar low density. Radioligand binding studies revealed for both cytokines approximately 300 receptors/cell with similar high affinity. An additional class of IL-13Rs was identified after occupation of the shared high-affinity receptors by the nonsignaling, double-mutant IL-4121R-->D, 124Y-->D (R.Y. \*\*\*IL\*\*\* - \*\*\*4\*\*\* ). In these experiments, 1251-IL-13 bound to a single receptor population with a Kd of approximately 300 pM and approximately 5000 sites/cell, matching the published affinity of monomeric IL-13Ralpha2 when expressed in COS7 cells.

R.Y. \*\*\*IL\*\*\* - \*\*\*4\*\*\* blocked the \*\*\*IL\*\*\* - \*\*\*4\*\*\* - and IL-13-mediated vascular cell adhesion molecule (VCAM)-1 expression and Stat6 activation, suggesting that the large number of high-affinity IL-13Ralpha2 monomers are silent receptors, likely representing a decoy target for IL-13.

L5 ANSWER 18 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

production is low or absent. On the other hand, IL-13 inhibits proinflammatory cytokine and chemokine production in vitro and has potent antiinflammatory activities in vivo. From these observations, it can be concluded that IL-13 is an antiinflammatory cytokine that plays a unique role in the induction and maintenance of IgE production and IgE-mediated allergic responses.

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L5 ANSWER 20 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
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L5 ANSWER 21 OF 82 MEDLINE  
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DOCUMENT NUMBER: 98256353  
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ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
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L5 ANSWER 23 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
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TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

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L5 ANSWER 24 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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L5 ANSWER 25 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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L5 ANSWER 26 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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L5 ANSWER 27 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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L5 ANSWER 28 OF 82 MEDLINE  
ACCESSION NUMBER: 1998256353 MEDLINE  
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TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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ACCESSION NUMBER: 1998256353 MEDLINE  
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AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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ACCESSION NUMBER: 1998256353 MEDLINE  
DOCUMENT NUMBER: 98256353  
TITLE: Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 act on human lung fibroblasts. Implication in asthma.

AUTHOR: Doucet C; Brouty-Boye D; Pottin-Clementeau C; Canonica G W; Jasnin C; Azzarone B

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CORPORATE SOURCE: U268 INSERM Hospital Paul Brousse, 94807 Villejuif Cedex, France.

SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1998 May 15) 101 (10) 2129-39.

Journal code: HS7. ISSN: 0021-9738.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 199808

ENTRY WEEK: 19980804

AB Airway hyperresponsiveness leading to subepithelial fibrosis is mediated by inflammatory cells activated by T helper (Th) 2-derived cytokines such as \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-5. By analyzing the phenotype and response of human lung fibroblasts derived from either fetal (ICIG7) or adult (CCL202) tissue as well as from a Th2-type stromal reaction (FPA) to \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13, we provide evidence that human lung fibroblasts may behave as inflammatory cells upon activation by \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13. We show that the three types of fibroblasts constitute different populations that display a distinct pattern in cell surface molecule expression and proinflammatory cytokine and chemokine release. All fibroblasts express functional but different \*\*\*IL\*\*\* .

\*\*\*4\*\*\* / \*\*\*IL\*\*\* . \*\*\*13\*\*\* \*\*\*receptors\*\*\* . Thus, while \*\*\*IL\*\*\* . \*\*\*4\*\*\* receptor (R) alpha and IL-13Ralpha1 chains are present in all the cells, CCL202 and FPA fibroblasts coexpress the IL-13Ralpha2 and the IL-2Rgamma chain, respectively, suggesting the existence of a heterotrimeric receptor (IL-4Ralpha/IL-13Ralpha/IL-2Rgamma) able to bind \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13. Stimulation with \*\*\*IL\*\*\* . \*\*\*4\*\*\* or IL-13 triggers in the fibroblasts a differential signal transduction and upregulation in the expression of beta1 integrin and vascular cell adhesion molecule 1 and in the production of IL-6 and monocyte chemoattractant protein 1, two inflammatory cytokines important in the pathogenesis of allergic inflammation. Our results suggest that when activated by \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13, different subsets of lung fibroblasts may act as effector cells not only in the pathogenesis of asthma but also in lung remodeling processes. They may also differentially contribute to trigger and maintain the recruitment, homing, and activation of inflammatory cells.

L5 ANSWER 19 OF 82 MEDLINE  
ACCESSION NUMBER: 1998250014 MEDLINE  
DOCUMENT NUMBER: 98250014  
TITLE: Novel way to increase targeting specificity to a human glioblastoma-associated receptor for interleukin 13.  
AUTHOR: Debinski W; Gibo D M; Puri R K  
CORPORATE SOURCE: Section of Neurosurgery, Pennsylvania State University College of Medicine, Hershey 17033-0850, USA.. wdebinski@PSGHS.EDU  
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1998 May 18) 76 (4) 547-51.  
Journal code: GQU. ISSN: 0020-7136.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199808  
ENTRY WEEK: 19980801  
AB Human brain cancers (gliomas) overexpress large numbers of a receptor for interleukin 13 (IL13), making this receptor an attractive target for anti-glioma therapies. We have recently proposed that the glioma-associated \*\*\*IL13\*\*\* \*\*\*receptor\*\*\* is different from the one expressed on some hemopoietic and somatic cells. In an attempt to identify an even more glioma-specific target, we have used

an antagonist of a related cytokine, \*\*\*IL4\*\*\* , which neutralizes the physiological effects of both IL13 and \*\*\*IL4\*\*\* on normal cells. Here we demonstrate that the \*\*\*IL4\*\*\* antagonist also counteracts the action of cytotoxins targeted to the \*\*\*IL13\*\*\* \*\*\*receptor\*\*\* on normal human cells. Importantly, the \*\*\*IL4\*\*\* antagonist does not inhibit IL13-based cytotoxins on glioma cells at all. Thus, the \*\*\*IL13\*\*\* \*\*\*receptor\*\*\* on glioma cells can be categorized as tumor-specific in the presence of an \*\*\*IL4\*\*\* antagonist. We conclude that \*\*\*IL13\*\*\* \*\*\*receptor\*\*\* -directed cytotoxins can be delivered to glioma cells without being cytotoxic to normal cells.

L5 ANSWER 20 OF 82 MEDLINE

ACCESSION NUMBER: 1998217192 MEDLINE

DOCUMENT NUMBER: 98217192

TITLE: An antagonistic \*\*\*IL\*\*\* . \*\*\*4\*\*\* mutant prevents type I allergy in the mouse: inhibition of the \*\*\*IL\*\*\* . \*\*\*4\*\*\* / \*\*\*IL\*\*\* . \*\*\*13\*\*\* \*\*\*receptor\*\*\*

system completely abrogates humoral immune response to allergen and development of allergic symptoms in vivo.

AUTHOR: Grunewald S M; Werthmann A; Schnarr B; Klein C E; Brocker E; Mohr M; Brombacher F; Sebald W; Duschl A  
CORPORATE SOURCE: Biozentrum, Physiologische Chemie II, Universitat Wurzburg, Germany.

SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Apr 15) 160 (8) 4004-9.

Journal code: IFB. ISSN: 0022-1767.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 199807

ENTRY WEEK: 19980702

AB We have analyzed in vivo effects of the murine \*\*\*IL\*\*\* . \*\*\*4\*\*\* mutant Q116D/Y119D (QY), which forms unproductive complexes with IL-4Ralpha and is an antagonist for \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13 in vitro. Treatment of BALB/c mice with QY during immunization with OVA completely inhibited synthesis of OVA-specific IgE and IgG1.

BALB/c-derived knockout mice lacking either \*\*\*IL\*\*\* . \*\*\*4\*\*\* or IL-4Ralpha also did not develop specific IgE or IgG1, but mounted a much stronger IgG2a and IgG2b response than wild-type mice. In contrast, QY treatment of normal BALB/c mice suppressed specific IgG2a, IgG2b, and IgG3 synthesis, which may indicate the development of tolerance toward the allergen. Associated with the lack of IgE synthesis in QY-treated wild-type mice and in \*\*\*IL\*\*\* . \*\*\*4\*\*\* (-/-) mice used as a control was the failure to develop immediate cutaneous hypersensitivity or anaphylactic shock upon rechallenge. Interestingly, QY treatment also inhibited humoral immune responses and allergic reactivity in SJL/J mice, a strain that did not produce IgE, but displayed IgE-independent mast cell degranulation mediated by specific IgG1. We conclude that QY inhibits Ag-specific humoral immune responses and allergic symptoms mediated either by IgE or IgG1. It needs to be clarified how QY abrogates synthesis of IgG2a, IgG2b, and IgG3, but the induction of tolerance toward nonhazardous protein Ags should be advantageous for therapy of atopic disorders and other Th2-dominated diseases.

L5 ANSWER 21 OF 82 MEDLINE  
ACCESSION NUMBER: 1998212024 MEDLINE  
DOCUMENT NUMBER: 98212024  
TITLE: Regulation of interleukin-13 receptor constituents on mature human B lymphocytes.

AUTHOR: Ogata H; Ford D; Kouttab N; King T C; Vita N; Minty A; Stoeckler J; Morgan D; Girasole C; Morgan J W; Maizel A L

CORPORATE SOURCE: Roger Williams Medical Center/Brown University, Providence, Rhode Island 02908, USA.

CONTRACT NUMBER: CA45148 (NCI) R29-DK49649 (NIDDK)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Apr 17) 273 (16) 9864-71.

Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199807

ENTRY WEEK: 19980704

AB Human B cells stimulated through both their immunoglobulin and CD40 receptors up-regulate 745 +/- 51 interleukin (IL)-13 ligand binding sites with an affinity of 0.91 +/- 0.08 nM within 24 h. IL-13 binds primarily to the IL-13Ralpha1 with subsequent sequestration of the IL-4Ralpha into the complex. IL-13Ralpha1 may also be found in those receptors capable of binding \*\*\*IL\*\*\* . \*\*\*4\*\*\* . gamma chain (gammac) participates in receptors capable of binding \*\*\*IL\*\*\* . \*\*\*4\*\*\* but is not found in association with bound IL-13. Dimeric receptors composed of the IL-4Ralpha complexed with either the IL-13Ralpha1 or gammac occur simultaneously within defined B cell populations. mRNAs for all receptor constituents are increased subsequent to immunoglobulin stimulation alone, while maximal expression of IL-13Ralpha1 is more dependent upon co-stimulation of immunoglobulin and CD40 receptors. mRNA levels for IL-13Ralpha1 vary over a wider range subsequent to surface stimulation than other receptor components. Although gammac is not bound to IL-13 in B cells under the conditions evaluated, it may influence IL-13 binding by competing with IL-13Ralpha1 for association/sequestration with the IL-13Ralpha2 does not participate in the \*\*\*IL\*\*\* . \*\*\*13\*\*\* \*\*\*receptor\*\*\* that is up-regulated upon activation of quiescent tonsillar B lymphocytes, although mRNA for the protein may be found in the centroblastic fraction of tonsillar cells.

L5 ANSWER 22 OF 82 MEDLINE

ACCESSION NUMBER: 97426445 MEDLINE

DOCUMENT NUMBER: 97426445

TITLE: An interleukin ( \*\*\*IL\*\*\* ). \*\*\*13\*\*\* \*\*\*receptor\*\*\*

lacking the cytoplasmic domain fails to transduce IL-13-induced signals and inhibits responses to \*\*\*IL\*\*\* . \*\*\*4\*\*\* .

AUTHOR: Orchansky P L; Ayres S D; Hilton D J; Schrauder J W  
CORPORATE SOURCE: The Biomedical Research Centre, 2222 Health Sciences Mall, University of British Columbia, Vancouver V6T 1Z3, Canada.. patricia@brc.ubc.ca

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Sep 5) 272 (36) 22940-7.

Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199712

ENTRY WEEK: 19971201

AB Interleukin (IL)-13 is a pleiotropic immunoregulatory cytokine that shares many, although not all, of the biological activities of \*\*\*IL\*\*\* . \*\*\*4\*\*\* . The overlapping biological properties of \*\*\*IL\*\*\* . \*\*\*4\*\*\* and IL-13 appear to be due to the existence of shared components of the receptors, and we and others showed that the \*\*\*IL\*\*\* . \*\*\*4\*\*\* receptor-alpha is involved in signal transduction paths activated by both.

We show here that expression of the \*\*\*IL\*\*\* -  
 \*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* -alpha in two factor-dependent cell lines,  
 the premyeloid  
 FD5 and the T lymphoid CT4.S, conferred the ability to  
 grow continuously  
 in response to IL-13; to respond to IL-13 with tyrosine  
 phosphorylation of  
 JAK1, Tyk2, IL-4Ralpha, IRS-2, and STAT6; and to  
 respond to \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* with tyrosine phosphorylation of Tyk2 in  
 addition to those  
 induced in parental cell lines. Expression of a truncated  
 \*\*\*IL\*\*\* -  
 \*\*\*13\*\*\* \*\*\*receptor\*\*\* -alpha that lacked the  
 cytoplasmic domain  
 demonstrated that this domain was essential for  
 IL-13-dependent growth and  
 phosphorylation of the above substrates. Expression of this  
 truncated  
 \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* also resulted  
 in an inhibition  
 of biochemical and biological responses to \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* that  
 was exacerbated by the presence of IL-13. These dominant  
 inhibitory  
 effects indicate that the extracellular domain of the  
 truncated \*\*\*IL\*\*\* -  
 \*\*\*13\*\*\* \*\*\*receptor\*\*\* competes with gammac for  
 complexes of  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* and the \*\*\*IL\*\*\* - \*\*\*4\*\*\*  
 receptor-alpha,  
 or, when itself bound to IL-13, competes with \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* for  
 the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor-alpha.

L5 ANSWER 23 OF 82 MEDLINE  
 ACCESSION NUMBER: 97408450 MEDLINE  
 DOCUMENT NUMBER: 97408450  
 TITLE: The related cytokines interleukin-13 and  
 interleukin-4 are  
 distinguished by differential production and  
 differential  
 effects on T lymphocytes.  
 AUTHOR: Minty A; Asselin S; Bensussan A; Shire D;  
 Vita N; Vyakarnam  
 A; Wijdenes J; Ferrara P; Caput D  
 CORPORATE SOURCE: Sanofi Recherche,  
 Lab' ege-Innopol, France..  
 adrian.minty@bis1.elfsanofi.fr  
 SOURCE: EUROPEAN CYTOKINE NETWORK,  
 (1997 Jun) 8 (2) 203-13.  
 Journal code: A56. ISSN: 1148-5493.  
 PUB. COUNTRY: France  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199712  
 ENTRY WEEK: 19971201  
 AB We have compared the production of the related  
 cytokines IL-13 and  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* by T lymphocytes, and the effects  
 of the two  
 cytokines on these cells. IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\*  
 production  
 differ in a number of respects. IL-13 is produced at higher  
 levels than  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* by activated T lymphocytes, and  
 its accumulation in  
 the culture medium can be more prolonged, corresponding  
 partly to  
 differential mRNA accumulation and partly to a preferential  
 depletion of  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* from the culture medium. Certain  
 inducing  
 combinations such as PMA and anti-CD28, stimulate high  
 levels of IL-13 and  
 IL-13 mRNA, but little or no \*\*\*IL\*\*\* - \*\*\*4\*\*\* or  
 \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* mRNA. The ratio of IL-13 to \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\*, both at  
 protein and mRNA levels, is higher in CD8+ lymphocyte  
 than in CD4+  
 lymphocyte populations. Although after in vitro polarization  
 of peripheral  
 blood lymphocytes leading to type 1 and type 2  
 populations, IL-13 is made  
 principally by cells of a type 2 phenotype, as is \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\*  
 ; it can also be produced by type 1 CD4+ and CD8+ T  
 lymphocyte clones  
 making large amounts of IFN-gamma and very little  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\*  
 . IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* exert different effects  
 on T  
 lymphocyte functions. IL-13 does not significantly inhibit  
 the  
 IL-2-induced T lymphocyte production of IFN-gamma,  
 RANTES, MIP-1 alpha or  
 MIP-1 beta, nor that of perforin mRNA, as does \*\*\*IL\*\*\* -

\*\*\*4\*\*\*  
 We have also been unable to demonstrate STAT6 activation  
 by IL-13 on T  
 lymphocytes purified in a number of ways, despite strong  
 activation of  
 STAT6 by \*\*\*IL\*\*\* - \*\*\*4\*\*\* in these cells. This is  
 contrary to some  
 previous reports, but is consistent with the notion that the  
 majority of T  
 lymphocytes lack functional \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptors\*\*\*  
 A higher and more prolonged T lymphocyte production of  
 IL-13 than that of  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* may thus be permissible because  
 IL-13 does not  
 inhibit T-cell functions. Conversely, sustained IL-13  
 production may be  
 partly due to the absence of receptor-mediated depletion of  
 this cytokine.

L5 ANSWER 24 OF 82 MEDLINE  
 ACCESSION NUMBER: 97321053 MEDLINE  
 DOCUMENT NUMBER: 97321053  
 TITLE: Chromosome mapping and expression of the  
 human  
 interleukin-13 receptor.  
 AUTHOR: Guo J; Apiou F; Mellerin M P; Lebeau B;  
 Jacques Y;  
 Minvielle S  
 CORPORATE SOURCE: INSERM U211, Institut de  
 Biologie, Nantes, France.  
 SOURCE: GENOMICS, (1997 May 15) 42 (1) 141-5.  
 Journal code: GEN. ISSN: 0888-7543.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-Y08768  
 ENTRY MONTH: 199709  
 ENTRY WEEK: 19970902  
 AB Interleukin-13 (IL-13) is a cytokine secreted by activated  
 T cells and  
 shares most but not all biological activities with interleukin-4  
 (  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* ). Both cytokines play an important  
 role as a switch  
 factor directing synthesis of IgE; they act on monocytes and  
 endothelial  
 cells, but unlike \*\*\*IL\*\*\* - \*\*\*4\*\*\* , IL-13 does not act  
 on T cells.  
 These cytokines have both common and distinct  
 components in their  
 respective receptors. Based on sequence similarity shared  
 by cytokine  
 receptor family members, we have identified a cDNA  
 encoding the human  
 \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* (IL-13R). This  
 cDNA was used to  
 examine the pattern of IL-13R mRNA expression by  
 Northern blot analyses of  
 poly(A)+ RNA purified from different human tissues and  
 cell lines. Among  
 several myeloma cell lines analyzed, the U266 cell line was  
 the only one  
 found to express IL-13R transcripts. This cell line is also the  
 only one  
 described as producing IgE. The IL-13R gene was mapped to  
 chromosome Xq24  
 by in situ hybridization. Interestingly, this locus is near that  
 of the  
 CD40 ligand gene, the product of which is also involved,  
 like IL-13, in  
 proliferation and IgE isotype switching of human B cells.  
 The human IL-13R  
 gene maps between two cytokine receptor genes located on  
 the chromosome  
 arm Xq region: the interleukin-2 receptor gamma chain gene  
 (Xq13.1) and  
 the interleukin-9 receptor gene (Xq28). The lack of  
 nucleotide sequence  
 similarity suggests unrelated evolutionary pathways  
 between these receptor  
 genes.

L5 ANSWER 25 OF 82 MEDLINE  
 ACCESSION NUMBER: 97238889 MEDLINE  
 DOCUMENT NUMBER: 97238889  
 TITLE: Identification, purification, and characterization  
 of a  
 soluble interleukin (IL)-13-binding protein.  
 Evidence that  
 it is distinct from the cloned \*\*\*IL\*\*\* -  
 \*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* and \*\*\*IL\*\*\* - \*\*\*4\*\*\*  
 receptor  
 alpha-chains.  
 AUTHOR: Zhang J G; Hilton D J; Willson T A;  
 McFarlane C; Roberts B  
 A; Moritz R L; Simpson R J; Alexander W S;  
 Metcalf D;

Nicola N A  
 CORPORATE SOURCE: Walter and Eliza Hall Institute of  
 Medical Research and the  
 Cooperative Research Centre for Cellular Growth  
 Factors,  
 P.O. Royal Melbourne Hospital, Victoria 3050,  
 Australia.  
 SOURCE: JOURNAL OF BIOLOGICAL  
 CHEMISTRY, (1997 Apr 4) 272 (14)  
 9474-80.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199707  
 AB Interleukin-4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) and  
 interleukin-13 (IL-13) are  
 structurally and functionally related cytokines which play an  
 important  
 role in the regulation of the immune response to infection.  
 The functional  
 similarity of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 can be  
 explained, at  
 least in part, by the common components that form their  
 cell surface  
 receptors, namely the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor  
 alpha-chain  
 (IL-4Ralpha) and the \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptor\*\*\*  
 alpha-chain (IL-13Ralpha). Soluble forms of the IL-4Ralpha  
 have also been  
 described and implicated in modulating the effect of  
 \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* . In this paper we describe the presence of a  
 45,000-50,000 Mr  
 IL-13-binding protein (IL-13BP) in the serum and urine of  
 mice. This  
 protein binds IL-13 with a 100-300-fold higher affinity (KD  
 = 20-90 pM)  
 than does the cloned IL-13Ralpha (KD = 3-10 nM). In  
 addition to this  
 functional difference, the IL-13BP appears to be structurally  
 and  
 antigenically distinct from the IL-13Ralpha. Finally, unlike  
 the cloned  
 receptor, the IL-13BP acts as a potent inhibitor of IL-13  
 binding to its  
 cell surface receptor, raising the possibility that it may be  
 used to  
 modulate the effects of IL-13 in vivo.

L5 ANSWER 26 OF 82 MEDLINE  
 ACCESSION NUMBER: 97190270 MEDLINE  
 DOCUMENT NUMBER: 97190270  
 TITLE: Tumor necrosis factor alpha enhances the  
 expression of the  
 interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* receptor  
 alpha-chain  
 on endothelial cells increasing \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* or  
 IL-13-induced Stat6 activation.  
 AUTHOR: Lugli S M; Feng N; Heim M H; Adam M;  
 Schnyder B; Etter H;  
 Yamane M; Eugster H P; Lutz R A; Zurawski G;  
 Moser R  
 CORPORATE SOURCE: Institute of Toxicology, Federal  
 Institute of Technology,  
 CH-8057 Zurich, Switzerland.  
 SOURCE: JOURNAL OF BIOLOGICAL  
 CHEMISTRY, (1997 Feb 28) 272 (9)  
 5487-94.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199706  
 AB Functional receptors for interleukin ( \*\*\*IL\*\*\* )-  
 \*\*\*4\*\*\* and IL-13  
 on endothelial cells consist of the 130-kDa \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\*  
 receptor alpha-chain (IL-4Ralpha) and a 65-75-kDa IL-13  
 binding subunit  
 that are expressed in a ratio of about 1:3, respectively. The  
 restricted  
 number of IL-4Ralpha limits subunit heterodimerization and  
 in turn  
 receptor-mediated signaling. We report here, the effects of  
 tumor necrosis  
 factor alpha (TNF-alpha) on the expression of the receptor  
 subunits for  
 \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13. By flow  
 cytometry and  
 receptor-binding analysis of iodinated \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* and IL-13,  
 stimulation with TNF-alpha-induced a 2-3-fold increase of  
 the IL-4Ralpha  
 expression. The up-regulation was also confirmed at the  
 transcriptional



level by reverse transcription-polymerase chain reaction. Radioligand cross-linking experiments revealed no change in the subunit composition of the TNF-alpha-induced receptor complex. Nevertheless, TNF-alpha stimulation led to increased activation of the \*\*\*IL\*\*\* - \*\*\*4\*\*\* -specific signal transducers and activators of transcription protein (Stat6) by \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13. Thus, TNF-alpha corrects the subunit imbalance of the endothelial \*\*\*IL\*\*\* - \*\*\*4\*\*\*. \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* complex thereby increasing receptor heterodimerization and in turn the signaling capability by \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13.

L5 ANSWER 27 OF 82 MEDLINE  
ACCESSION NUMBER: 97174273 MEDLINE  
DOCUMENT NUMBER: 97174273  
TITLE: X-SCID B cell responses to interleukin-4 and interleukin-13  
are mediated by a receptor complex that includes the interleukin-4 receptor alpha chain (p140) but not the gamma c chain.  
AUTHOR: Matthews D J; Hibbert L; Friedrich K; Minty A; Callard R E  
CORPORATE SOURCE: Immunobiology Unit, Institute of Child Health, London, GB.  
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Jan) 27 (1) 116-21.  
Journal code: EN5. ISSN: 0014-2980.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199705  
AB This study investigates the effect of interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* mutant proteins and a monoclonal antibody to the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor alpha chain on \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 response by B cells from X-linked severe combined immunodeficiency (X-SCID) patients in which the common gamma chain (gamma c chain) gene mutations have been fully characterized and no gamma c chain expression was detected. In this gamma c chain gene knockout model, it was confirmed that the gamma c chain is essential for B cell responses to IL-2 but not for \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13. Dose-response curves for X-SCID and normal B cell responses to \*\*\*IL\*\*\* - \*\*\*4\*\*\* were indistinguishable, showing that the loss of the gamma c chain did not diminish the sensitivity of B cells to \*\*\*IL\*\*\* - \*\*\*4\*\*\*. The mutant protein \*\*\*IL\*\*\* - \*\*\*4\*\*\* (Y124D) and an antibody to the IL-4R alpha chain both inhibited responses of X-SCID B cells to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13, showing that X-SCID B cell responses to these cytokines are mediated by a receptor complex that includes the IL-4R alpha chain but not the gamma c chain. Another mutant protein, \*\*\*IL\*\*\* - \*\*\*4\*\*\* (R88D), which has greatly reduced affinity for IL-4R alpha, was found to inhibit responses by normal B cells to \*\*\*IL\*\*\* - \*\*\*4\*\*\* but not to IL-13. \*\*\*IL\*\*\* - \*\*\*4\*\*\* (R88D), did not, however, inhibit X-SCID B cell responses to \*\*\*IL\*\*\* - \*\*\*4\*\*\*. This result is consistent with \*\*\*IL\*\*\* - \*\*\*4\*\*\* (R88D) inhibition of responses mediated by receptor complexes that include the gamma c chain. We propose that X-SCID B cells responses to \*\*\*IL\*\*\* - \*\*\*4\*\*\* are mediated by an \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* complex comprised of the IL-4R alpha chain associated with the recently cloned IL-13R binding protein. This model has major implications for understanding normal B cell responses to \*\*\*IL\*\*\* - \*\*\*4\*\*\*.

L5 ANSWER 28 OF 82 MEDLINE

ACCESSION NUMBER: 97165986 MEDLINE  
DOCUMENT NUMBER: 97165986  
TITLE: Cloning of the human IL-13R alpha1 chain and reconstitution with the IL4R alpha of a functional \*\*\*IL\*\*\* - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* complex.  
AUTHOR: Miloux B; Laurent P; Bonnin O; Lupker J; Caput D; Vita N; Ferrara P  
CORPORATE SOURCE: Sanofi Recherche, Lab' ege Innopole, France.  
SOURCE: FEBS LETTERS, (1997 Jan 20) 401 (2-3) 163-6.  
Journal code: EUH. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
OTHER SOURCE: GENBANK-Y09328  
ENTRY MONTH: 199705  
AB The human homologue of the recently cloned murine IL-13 binding protein (IL-13R alpha1) was cloned from a cDNA library derived from the carcinoma cell line CAKI-1. The cloned cDNA encodes a 427 amino acid protein with two consensus patterns characteristic of the hematopoietic cytokine receptor family and a short cytoplasmic tail. The human protein is 74% identical to the murine IL-13R alpha1, and 27% identical to the human IL-13R alpha2. CHO cells expressing recombinant hIL-13R alpha1 specifically bind IL-13 (Kd approximately 4 nM) but not \*\*\*IL\*\*\* - \*\*\*4\*\*\*. Co-expression of the cloned cDNA with that of IL-4R alpha resulted in a receptor complex that displayed high affinity for IL-13 (Kd approximately 30 pM), and that allowed cross-competition of IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\*. Electrophoretic mobility shift assay showed that IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* were able to activate Stat6 in cells expressing both IL-4R alpha and IL-13R alpha1, while no activation was observed in cells expressing either one or the other alone.

L5 ANSWER 29 OF 82 MEDLINE  
ACCESSION NUMBER: 97164670 MEDLINE  
DOCUMENT NUMBER: 97164670  
TITLE: Interleukin (IL)-10, but not \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13, inhibits cytokine production and growth in juvenile myelomonocytic leukemia cells.  
AUTHOR: Iversen P O; Hart P H; Bonder C S; Lopez A F  
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, IMVS, Adelaide, Australia.  
SOURCE: CANCER RESEARCH, (1997 Feb 1) 57 (3) 476-80.  
Journal code: CNF. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199704  
AB Juvenile myelomonocytic leukemia (JMML) carries a poor prognosis. The endogenous production of cytokines by the JMML cells contributes to their growth and therapeutic resistance. Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\*, IL-10, and IL-13 inhibit cytokine production in monocytes. We have now studied whether these cytokines can inhibit JMML cell cytokine production, thereby potentially reducing the malignant cell load in this disorder. We found that IL-10, but not \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13, dose dependently inhibited JMML cell production of the hemopoietic growth factors granulocyte-macrophage colony-stimulating factor, tumor necrosis factor alpha, and IL-1beta. Similarly, IL-10, but not \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13, suppressed JMML colony formation and cell viability. This was not due to the absence of receptors because we could detect mRNAs for the \*\*\*IL\*\*\* - \*\*\*4\*\*\* and the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* alpha subunits and the IL-2 common

gamma subunit in JMML cells. Furthermore, the receptors were active since both \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 up-regulated surface expression of MHC class II and down-regulated CD14 antigens on JMML cells and monocytes. Unlike activated monocytes, the JMML cells did not produce IL-10. It is suggested that the loss of cytokine inhibitory effects of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 could play a role in the pathogenesis of this disorder. On the other hand, the inhibition of cytokine production, growth, and viability of JMML cells by IL-10 suggests that this cytokine may have a therapeutic potential in JMML.

L5 ANSWER 30 OF 82 MEDLINE  
ACCESSION NUMBER: 97162178 MEDLINE  
DOCUMENT NUMBER: 97162178  
TITLE: Human ovarian-carcinoma cell lines express \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\* : comparison between \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13-induced signal transduction.  
AUTHOR: Murata T; Obiri N I; Puri R K  
CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD 20892, USA.  
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1997 Jan 17) 70 (2) 230-40.  
Journal code: GQU. ISSN: 0020-7136.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199704  
AB We have reported that human ovarian-carcinoma cell lines express high-affinity \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor. Since IL-4R has been hypothesized to share a chain with IL-13R, we investigated whether ovarian cancer cells express \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\*. In the present study, we report that the ovarian-carcinoma cell lines IGROV-1 and PA-1 express varying numbers of high-affinity \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\*. Furthermore, IL-13 inhibited the binding of \*\*\*IL\*\*\* - \*\*\*4\*\*\* on both ovarian-carcinoma cell lines, while \*\*\*IL\*\*\* - \*\*\*4\*\*\* did not inhibit IL-13 binding on IGROV-1 cell line. IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* induced the phosphorylation of JAK1, JAK2 and Tyk2 Janus kinases in PA-1 cells. In contrast, JAK3 tyrosine kinase was expressed in PA-1 cells, but \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13 did not augment its phosphorylation. In IGROV-1 cells, Tyk2 was constitutively phosphorylated and this phosphorylation was augmented by \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13. JAK1 and JAK2 but not JAK3 were expressed but only JAK2 was faintly phosphorylated in response to either IL-13 or \*\*\*IL\*\*\* - \*\*\*4\*\*\* respectively. IRS (insulin-receptor substrate)-1 and IRS-2 were also phosphorylated constitutively in both ovarian cancer cell lines examined, but only the phosphorylation of IRS-1 was augmented in response to \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13. STAT6 was phosphorylated and activated in response to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 in all lines examined. Our results demonstrate that ovarian cancer cell lines may express 2 types of IL-13R and the IL-13- or \*\*\*IL\*\*\* - \*\*\*4\*\*\* -induced signaling patterns may be slightly different in each type of receptor.

L5 ANSWER 31 OF 82 MEDLINE  
ACCESSION NUMBER: 97146045 MEDLINE  
DOCUMENT NUMBER: 97146045  
TITLE: The \*\*\*IL\*\*\* - \*\*\*13\*\*\*

\*\*\*receptor\*\*\* structure differs on various cell types and may share more than one component with \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor.

AUTHOR: Obiri N I; Leland P; Murata T; Debinski W; Puri R K  
 CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Food and Drug Administration, Center for Biologics Evaluation and Research, Bethesda, MD 20892, USA.  
 SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Jan 15) 158 (2) 756-64.  
 Journal code: IFB. ISSN: 0022-1767.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
 ENTRY MONTH: 199704  
 AB We have reported on the expression and characteristics of IL-13R and have demonstrated that IL-13 competes for \*\*\*IL\*\*\* - \*\*\*4\*\*\* binding while \*\*\*IL\*\*\* - \*\*\*4\*\*\* did not compete for the IL-13 binding on some cell types. Based on these observations, and the size of IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* cross-linked proteins, we concluded that the receptor for IL-13 is complex and shares a subunit with the receptor for \*\*\*IL\*\*\* - \*\*\*4\*\*\*. To explore the complexity of the IL-13R, a wide variety of cell types was examined for IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* binding. We report in this work that \*\*\*IL\*\*\* - \*\*\*4\*\*\* does not always bind well to cells that bind IL-13, but the reverse is also true. We also found that \*\*\*IL\*\*\* - \*\*\*4\*\*\* can compete more effectively for IL-13 binding than IL-13 itself. Cross-linking studies support these observations and demonstrate that 125I-labeled IL-13 bound exclusively to a single 65- to 70-kDa protein in MA-RCC and U251 cells, while in TF-1 cells it cross-linked to two membrane proteins of 65 to 70 kDa and 140 kDa. Furthermore, by using a chimeric protein composed of IL-13 and Pseudomonas exotoxin A, we observed that \*\*\*IL\*\*\* - \*\*\*4\*\*\* neutralized the cytotoxicity of the IL-13 toxin on COS-7 cells by blocking a common form of the two cytokine receptors. We propose that the 65- to 70-kDa form of the IL-13R is the predominant common component shared between IL-13 and IL-4R. However, the primary \*\*\*IL\*\*\* - \*\*\*4\*\*\* binding (p140) protein also participates in the formation of the IL-13R complex in some cell types. In addition, the gamma(c) or another interactive subunit may influence IL-13 binding to its receptor complex. Thus, we propose that there are at least four forms of IL-13R.

L5 ANSWER 32 OF 82 MEDLINE  
 ACCESSION NUMBER: 97079260 MEDLINE  
 DOCUMENT NUMBER: 97079260  
 TITLE: Interleukin-13 is a potent activator of JAK3 and STAT6 in cells expressing interleukin-2 receptor-gamma and interleukin-4 receptor-alpha.  
 AUTHOR: Malabarba M G; Rui H; Deutsch H H; Chung J; Kalithoff S; Farrar W L; Kirken R A  
 CORPORATE SOURCE: Division of Basic Science, IRSP, SAIC Frederick, MD, USA.  
 SOURCE: BIOCHEMICAL JOURNAL, (1996 Nov 1) 319 ( Pt 3) 865-72.  
 Journal code: 9YO. ISSN: 0264-6021.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199703  
 AB The lymphocyte growth factors interleukin-2 (IL2), \*\*\*IL4\*\*\*, IL7, IL9 and IL15 use the common IL2 receptor-gamma (IL2R gamma) and activate the IL2R gamma-associated tyrosine kinase JAK3 (Janus kinase 3). IL13 is

structurally related to \*\*\*IL4\*\*\*, competes with \*\*\*IL4\*\*\* for binding to cell surface receptors and exhibits many similar biological effects. The molecular basis for this functional overlap between \*\*\*IL4\*\*\* and IL13 has been attributed mainly to a shared use of the 140 kDa IL4R alpha, since these cytokines appear to be uniquely different in that, according to several recent reports, IL13 does not recruit the IL2R gamma or JAK3. This notion has been supported by the identification of a novel 70 kDa \*\*\*IL13\*\*\* \*\*\*receptor\*\*\* in certain IL13-responsive cell lines that lack IL2R gamma. The present study sheds new light on the issue of functional overlap between IL13 and \*\*\*IL4\*\*\*, by demonstrating for the first time that, in cells that express both IL2R gamma and IL4R alpha, IL13 can mimic \*\*\*IL4\*\*\*-induced heterodimerization of IL2R gamma and IL4R alpha, with consequent marked activation of JAK3 and the transcription factor STAT6 (\*\*\*IL4\*\*\*-STAT). Reconstitution experiments in BA/F3 cells showed that both cytokines require the simultaneous presence of IL4R alpha and IL2R gamma to mediate JAK3 and proliferative responses, and analysis of 12 IL4R alpha variants showed that \*\*\*IL4\*\*\* and IL13 signals were equally affected by mutations of the cytoplasmic domain. We conclude that IL13 activates the IL2R gamma-associated JAK3 tyrosine kinase in appropriate cell types, and propose that IL13 is capable of interacting with multiple receptor subunits in a cell-dependent and combinatorial manner. Consequently, we predict that partial disruption of IL13 signal transduction also contributes to the severe combined immuno-deficiency syndromes associated with inactivation of the IL2R gamma or JAK3 genes.

L5 ANSWER 33 OF 82 MEDLINE  
 ACCESSION NUMBER: 97067184 MEDLINE  
 DOCUMENT NUMBER: 97067184  
 TITLE: cDNA cloning and characterization of the human interleukin 13 receptor alpha chain.  
 AUTHOR: Aman M J; Tayebi N; Obiri N I; Puri R K; Modi W S; Leonard W J  
 CORPORATE SOURCE: Laboratory of Molecular Immunology, NHLBI, National Institutes of Health, Bethesda, Maryland 20892-1674, USA.  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Nov 15) 271 (46) 29265-70.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 OTHER SOURCE: GENBANK-U62858  
 ENTRY MONTH: 199703  
 ENTRY WEEK: 19970302  
 AB We have cloned cDNAs corresponding to the human interleukin 13 receptor alpha chain (IL-13Ralpha). The protein has 76% homology to murine IL-13Ralpha, with 95% amino acid identity in the cytoplasmic domain. Only weak IL-13 binding activity was found in cells transfected with only IL-13Ralpha; however, the combination of both IL-13Ralpha and IL-4Ralpha resulted in substantial binding activity, with a Kd of approximately 400 pM, indicating that both chains are essential components of the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\*. Whereas IL-13Ralpha serves as an alternative accessory protein to the common cytokine receptor gamma chain (gamma(c)) for \*\*\*IL\*\*\* - \*\*\*4\*\*\* signaling, it could not replace the function of gamma(c) in allowing enhanced IL-2 binding activity. Nevertheless, the overall size and length of the cytoplasmic domain of IL-13Ralpha and gamma(c) are similar, and like gamma(c), IL-13Ralpha is

located on chromosome X.

L5 ANSWER 34 OF 82 MEDLINE  
 ACCESSION NUMBER: 97042342 MEDLINE  
 DOCUMENT NUMBER: 97042342  
 TITLE: Interleukin-4-specific signal transduction events are driven by homotypic interactions of the interleukin-4 receptor alpha subunit.  
 AUTHOR: Lai S Y; Molden J; Liu K D; Puck J M; White M D; Goldsmith M A  
 CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, University of California, San Francisco, USA.  
 CONTRACT NUMBER: GM54351-01 (NIGMS)  
 SOURCE: EMBO JOURNAL, (1996 Sep 2) 15 (17) 4506-14.  
 Journal code: EMB. ISSN: 0261-4189.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199703  
 AB Interleukin-4 (\*\*\*IL\*\*\* - \*\*\*4\*\*\*) exerts its effects through a heterodimeric receptor complex (IL-4R), which contains the IL-4R(alpha) and gamma(c) subunits. IL-4R(alpha) also functions with other partner subunits in several receptor types, including the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\*. To examine the roles of the individual subunits within IL-4R complexes, we employed a chimeric system that recapitulates native IL-4R function as verified by the activation of the kinases, JAK1 and JAK3, and induction of STAT-6. When a mutant gamma(c) subunit in which the four cytoplasmic tyrosines were converted to phenylalanine was paired with the cytoplasmic domain of the IL-4R(alpha) chain, specificity within the JAK-STAT pathway was not altered. Signaling events were examined further in cells expressing the IL-4R(alpha) chimera alone without the gamma(c) chimera. Ligand-induced homodimerization of these receptors activated the \*\*\*IL\*\*\* - \*\*\*4\*\*\* signaling program despite the absence of gamma(c), including induction of JAK1 and STAT-6, phosphorylation of the insulin-related substrate 1 and cellular proliferation. Thus, homotypic interactions of the IL-4R(alpha) subunit are sufficient for the initiation and determination of \*\*\*IL\*\*\* - \*\*\*4\*\*\*-specific signaling events, and such interactions may be integral to signaling through IL-4R complexes.

L5 ANSWER 35 OF 82 MEDLINE  
 ACCESSION NUMBER: 97024821 MEDLINE  
 DOCUMENT NUMBER: 97024821  
 TITLE: Modulation of the human IgE response.  
 AUTHOR: de Vries J E; Yssel H  
 CORPORATE SOURCE: Human Immunology Dept, DNAX Research Institute for Molecular and Cellular Biology, Palo Alto, CA, USA.  
 SOURCE: EUROPEAN RESPIRATORY JOURNAL. SUPPLEMENT, (1996 Aug) 22 58s-62s. Ref: 35  
 Journal code: ACK. ISSN: 0904-1850.  
 PUB. COUNTRY: Denmark  
 Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199703  
 ENTRY WEEK: 19970304  
 AB Studies on the immunological basis of allergic diseases have indicated that enhanced production of the cytokines interleukin (\*\*\*IL\*\*\* - \*\*\*4\*\*\*) and IL-13 and the reduced production of interferon-gamma (IFN-gamma) by allergen-specific T-cells contribute to enhanced immunoglobulin E (IgE) synthesis and the development of allergic disease in certain individuals. Therefore, inhibition of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 synthesis or blocking of activities of these cytokines would be

one approach to inhibiting IgE production. In the present communication, novel approaches toward this goal are discussed. It is shown that an

\*\*\*[L\*\*\* . \*\*\*4\*\*\* mutant protein, in which the tyrosine residue at position 124 is replaced by aspartic acid ( \*\*\*[L\*\*\* . \*\*\*4\*\*\* ,Y124D), binds with high affinity to the \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor, without receptor activation. \*\*\*[L\*\*\* . \*\*\*4\*\*\* ,Y124D acts as a potent antagonist both of \*\*\*[L\*\*\* . \*\*\*4\*\*\* and IL-13 activity in vitro, and inhibits immunoglobulin G4 (IgG4) and IgE production induced by these cytokines. These data are compatible with the notion that the \*\*\*[L\*\*\* . \*\*\*4\*\*\* and \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptors\*\*\* are complex receptors, which share a common component, which is required for signal transduction. In addition, it has been demonstrated that allergen-specific T-cells, belonging to the T-helper 2 (Th2) subset can be rendered anergic after incubation with allergen-derived peptides representing minimal T-cell activation inducing epitopes. These anergic Th2 cells failed to produce \*\*\*[L\*\*\* . \*\*\*4\*\*\* and IL-13, and failed to proliferate after activation with allergen and antigen-presenting cells (APC). The energized T cells also failed to give B-cells help in IgE synthesis, although they expressed normal levels of the CD40 ligand (CD40L). Exogenous \*\*\*[L\*\*\* . \*\*\*4\*\*\* and IL-13 failed to restore IgE synthesis, indicating that in addition to CD40L other co-stimulatory signals are required for productive T-cell/B-cell interactions, resulting in IgE synthesis. IgE production was restored by exogenous IL-2, demonstrating that IL-2 reverses the nonresponsive state and helper function of these nonresponsive T-cells. It is tempting to speculate that induction of T-cell nonresponsiveness by allergen-derived peptides may represent the underlying mechanisms for successful immunotherapy in allergic patients.

L5 ANSWER 36 OF 82 MEDLINE  
ACCESSION NUMBER: 97017071 MEDLINE  
DOCUMENT NUMBER: 97017071  
TITLE: Biochemical and morphological characterization of vascular and lymphocytic interleukin-4 receptors.  
AUTHOR: Schnyder B; Lugli S M; Schnyder-Candrian S; Eng V M; Moser R; Banchereau J; Ryffel B; Car B D  
CORPORATE SOURCE: Institute of Toxicology, Swiss Federal Institute of Technology-ETH, Schwerzenbach, Switzerland.  
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1996 Oct) 149 (4) 1369-79.  
Journal code: 3RS. ISSN: 0002-9440.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
ENTRY MONTH: 199702  
AB The distribution of the interleukin ( \*\*\*[L\*\*\* )- \*\*\*4\*\*\* receptor in normal human and common marmoset (Callithrix jacchus) tissues was examined by immunofluorescence and flow cytometry using monoclonal antibodies specific for the human \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor to gain further insight into \*\*\*[L\*\*\* . \*\*\*4\*\*\* -mediated inflammatory and immunological events. \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor positivity was unequivocally demonstrated on lymphocytes, predominantly T cells, and on blood vessels in many tissues. Vascular \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor immunofluorescence consisted of a strong smooth muscle cell positivity and weaker positive staining of capillary and venular endothelial cells. Subnanomolar concentrations of \*\*\*[L\*\*\* . \*\*\*4\*\*\* induced a

genistein-sensitive up-regulation of VCAM-1 in vascular cell cultures. Tumor necrosis factor-alpha induced a genistein-resistant up-regulation of VCAM-1. \*\*\*[L\*\*\* . \*\*\*4\*\*\* strongly induced expression of the \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor on splenocytes (T lymphocytes) but not on vascular smooth muscle or endothelial cell cultures. Receptor cross-linking to [125I] \*\*\*[L\*\*\* . \*\*\*4\*\*\* revealed a 65- to 75-kDa accessory receptor subunit consistent with a recently cloned \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptor\*\*\* associated with the \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor on both vascular endothelial and smooth muscle cells. The demonstration of a vascular distribution pattern for the \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor in addition to expression on lymphocytes suggests that vascular functional alterations, transduced through a unique \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor complex (the type II \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor), may be of importance during immunological and allergic inflammatory events.

L5 ANSWER 37 OF 82 MEDLINE  
ACCESSION NUMBER: 96417475 MEDLINE  
DOCUMENT NUMBER: 96417475  
TITLE: \*\*\*[L\*\*\* . \*\*\*4\*\*\* and \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptors\*\*\* : are they one and the same?.  
AUTHOR: Callard R E; Matthews D J; Hibbert L  
CORPORATE SOURCE: Immunobiology Unit, Institute of Child Health, London, UK.  
rcallard@ICH.BPMF.AC.UK  
SOURCE: IMMUNOLOGY TODAY, (1996 Mar) 17 (3) 108-10. Ref: 33  
Journal code: AEA. ISSN: 0167-5699.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
ENTRY MONTH: 199702  
AB Interleukin 4 ( \*\*\*[L\*\*\* . \*\*\*4\*\*\* ) and IL-13 share several biological properties, suggesting that they also share a common receptor or receptor component. Indeed, as discussed here by Robin Callard and colleagues, the \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptor\*\*\* appears to be a functional receptor for \*\*\*[L\*\*\* . \*\*\*4\*\*\* .

L5 ANSWER 38 OF 82 MEDLINE  
ACCESSION NUMBER: 96397528 MEDLINE  
DOCUMENT NUMBER: 96397528  
TITLE: \*\*\*[L4\*\*\* and \*\*\*[L13\*\*\* \*\*\*receptors\*\*\* share the gamma c chain and activate STAT6, STAT3 and STAT5 proteins in normal human B cells.  
AUTHOR: Rolling C; Treton D; Pellegrini S; Galanaud P; Richard Y  
CORPORATE SOURCE: INSERM U131, Institut Paris-Sud sur les Cytokines, Clamart, France.  
SOURCE: FEBS LETTERS, (1996 Sep 9) 393 (1) 53-6.  
Journal code: EUH. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199701  
AB IL13 induces the same biological effects as \*\*\*[L4\*\*\* in normal human B cells. We show that as in the IL4R complex, both IL4R alpha and IL2R gamma c are components of the IL13R and that both cytokines induced STAT6, STAT3 and STAT5 activation in B cells. In spite of this similar downstream signalling, \*\*\*[L4\*\*\* and IL13 used a different set of Janus kinases: IL13 is unable to activate JAK1 and JAK3.

L5 ANSWER 39 OF 82 MEDLINE  
ACCESSION NUMBER: 96357185 MEDLINE  
DOCUMENT NUMBER: 96357185  
TITLE: Inhibition of proliferation and clonal growth of human breast cancer cells by interleukin 13.  
AUTHOR: Serve S; Oelmann E; Herweg A; Oberberg D; Serve S; Reufi B; Mucke C; Minty A; Thiel E; Berdel W E

CORPORATE SOURCE: Department of Hematology and Oncology, Universitaetsklinikum Benjamin Franklin, Freie Universitaet, Hindenburgdamm, Berlin, Germany.  
CANCER RESEARCH, (1996 Aug 1) 56 (15) 3583-8.  
Journal code: CNF. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199612  
AB We tested the influence of recombinant human interleukin (rhIL)-13 and rhIL-4 on clonal growth of human breast cancer cell lines. rhIL-13 and rhIL-4 inhibited clonal growth of three of nine lines to approximately 50% of controls (ED50, 0.5 ng/ml). rhIL-13 reduced [3H]thymidine incorporation in all three cell lines: two showing a minor (84% and 83% of controls) and one showing a major response (25% of control). Both cytokines markedly reduced serum-induced G(0)/1 exit (approximately 25% versus 60%). 125I-labeled interleukin (IL) 13 binding assays revealed high-affinity binding sites for IL-13 on two of the three responding cell lines (KD approximately 60 pM). (Y124D) \*\*\*[L\*\*\* . \*\*\*4\*\*\* effectively antagonized all effects of rhIL-13 and rhIL-4, arguing for shared receptor components between them. However, neither rhIL-4 nor (Y124D) \*\*\*[L\*\*\* . \*\*\*4\*\*\* could displace 125I-labeled IL-13 from binding, although unlabeled rhIL-13 effectively did so. Using reverse transcription-PCR, we studied the expression of the common gamma chain (gamma c) in responding cell lines, putatively being shared between \*\*\*[L\*\*\* . \*\*\*4\*\*\* receptor and \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptor\*\*\* ; none of the three cell lines express gamma c. In conclusion, we demonstrate antiproliferative effects of \*\*\*[L\*\*\* . \*\*\*4\*\*\* and IL-13 on carcinoma cells which express IL-13 binding sites without participation of gamma c.  
L5 ANSWER 40 OF 82 MEDLINE  
ACCESSION NUMBER: 96343858 MEDLINE  
DOCUMENT NUMBER: 96343858  
TITLE: Differentiation and stability of T helper 1 and 2 cells derived from naive human neonatal CD4+ T cells, analyzed at the single-cell level.  
AUTHOR: Somasse T; Larenas P V; Davis K A; de Vries J E; Yssel H  
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute, Palo Alto, California 94304, USA.  
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Aug 1) 184 (2) 473-83.  
Journal code: I2V. ISSN: 0022-1007.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199611  
AB The development of CD4+ T helper (Th) type 1 and 2 cells is essential for the eradication of pathogens, but can also be responsible for various pathological disorders. Therefore, modulation of Th cell differentiation may have clinical utility in the treatment of human disease. Here, we show that interleukin (IL) 12 and \*\*\*[L\*\*\* . \*\*\*4\*\*\* directly induce human neonatal CD4+ T cells, activated via CD3 and CD28, to differentiate into Th1 and Th2 subsets. In contrast, IL-13, which shares many biological activities with \*\*\*[L\*\*\* . \*\*\*4\*\*\* , failed to induce T cell differentiation, consistent with the observation that human T cells do not express \*\*\*[L\*\*\* . \*\*\*13\*\*\* \*\*\*receptors\*\*\* . Both the IL-12-induced Th1 subset and the \*\*\*[L\*\*\* . \*\*\*4\*\*\* -induced Th2 subset produce large quantities of IL-10, confirming that human IL-10 is

not a typical human Th2 cytokine. Interestingly, \*\*\*IL\*\*\*  
 -driven Th2 cell differentiation was completely prevented by  
 an \*\*\*IL\*\*\*  
 - mutant protein ( \*\*\*IL\*\*\* . \*\*\*\*\*)  
 .Y124D), indicating  
 that this molecule acts as a strong \*\*\*IL\*\*\* . \*\*\*\*\*)  
 receptor  
 antagonist. Analysis of single T cells producing interferon  
 gamma or  
 \*\*\*IL\*\*\* . \*\*\*\*\*) revealed that induction of Th1 cell  
 differentiation  
 occurred rapidly and required only 4 d of priming of the  
 neonatal CD4+ T  
 cells in the presence of IL-12. The IL-12-induced Th1 cell  
 phenotype was  
 stable and was not significantly affected when repeatedly  
 stimulated in  
 the presence of recombinant \*\*\*IL\*\*\* . \*\*\*\*\*) . In  
 contrast, the  
 differentiation of Th2 cells occurred slowly and required not  
 only 6 d of  
 priming, but also additional restimulation of the primed  
 CD4+ T cells in  
 the presence of \*\*\*IL\*\*\* . \*\*\*\*\*) . Moreover,  
 \*\*\*IL\*\*\* . \*\*\*\*\*)  
 -induced Th2 cell phenotypes were not stable and could  
 rapidly be reverted  
 into a population predominantly containing Th0 and Th1  
 cells, after a  
 single restimulation in the presence of IL-12. The observed  
 differences in  
 stability of IL-12- and \*\*\*IL\*\*\* . \*\*\*\*\*) -induced  
 human Th1 and Th2  
 subsets, respectively, may have implications for  
 cytokine-based therapies  
 of chronic disease.

L5 ANSWER 41 OF 82 MEDLINE  
 ACCESSION NUMBER: 96303258 MEDLINE  
 DOCUMENT NUMBER: 96303258  
 TITLE: RU 41 740 (Biotin) and \*\*\*IL\*\*\* .  
 \*\*\*\*\*) , or IL-13,  
 have opposite effects on CD14, CD23, HLA-DR  
 and HLA-DQ on  
 monocytes.  
 AUTHOR: Garin L; Bemaud J; Picot N; Salvi M;  
 Corallo F; Bloy C;  
 Rigal D  
 CORPORATE SOURCE: Laboratoire d'Immunologie, Centre  
 Regional de Transfusion  
 Sanguine de Lyon, France.  
 SOURCE: INTERNATIONAL JOURNAL OF  
 IMMUNOPHARMACOLOGY, (1996 Jan) 18  
 (1) 69-74.  
 Journal code: GRI. ISSN: 0192-0561.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199704  
 ENTRY WEEK: 19970401  
 AB RU 41 740 (Biotin) is a glycoprotein extract obtained  
 from Klebsiella  
 pneumoniae. Its immunostimulating properties on  
 monocytes have been  
 established in vivo and in vitro. To confirm its spectrum of  
 action at  
 molecular level we studied its role on the modulation of four  
 molecules  
 involved in antigen presentation (HLA-DR, HLA-DQ),  
 uptake of endotoxin  
 (CD14) and activation (CD23). These four molecules are  
 known to be  
 modulated by interleukins \*\*\*IL\*\*\* . \*\*\*\*\*) and  
 IL-13. We found  
 that HLA-DR, HLA-DQ, CD14 and CD23 were  
 differentially regulated by  
 biotin and \*\*\*IL\*\*\* . \*\*\*\*\*) or IL-13. Surprisingly,  
 Biotin  
 inhibited the \*\*\*IL\*\*\* . \*\*\*\*\*) or IL-13-induced  
 expression of  
 CD23, HLA-DQ and HLA-DR, while it did not have any  
 action on these  
 molecules by itself. We therefore hypothesize that Biotin,  
 through the  
 action on its receptor, could interact with the \*\*\*IL\*\*\* .  
 \*\*\*\*\*)  
 receptor and \*\*\*IL\*\*\* . \*\*\*\*\*) \*\*\*receptor\*\*\*  
 and/or inhibit  
 the \*\*\*IL\*\*\* . \*\*\*\*\*) and \*\*\*IL\*\*\* . \*\*\*\*\*)  
 \*\*\*receptor\*\*\* transducing signal.

L5 ANSWER 42 OF 82 MEDLINE  
 ACCESSION NUMBER: 96151984 MEDLINE  
 DOCUMENT NUMBER: 96151984  
 TITLE: Interleukin-13 inhibits interleukin-2-induced  
 proliferation  
 and protects chronic lymphocytic leukemia B cells  
 from in

vitro apoptosis.  
 AUTHOR: Chaouchi N; Wallon C; Goujard C; Tertian  
 G; Rudant A; Caput  
 D; Ferrera P; Minty A; Vazquez A; Delfraissy J F  
 CORPORATE SOURCE: Laboratoire Virus Neurone et  
 Immunite, Faculte de Medecine  
 Paris Sud, France.  
 SOURCE: BLOOD, (1996 Feb 1) 87 (3) 1022-9.  
 Journal code: A8G. ISSN: 0006-4971.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals;  
 Priority Journals; Cancer  
 Journals  
 ENTRY MONTH: 199605  
 AB Human interleukin-13 (IL-13) acts at different stages of  
 the normal B-cell  
 maturation pathway with a spectrum of biologic activities  
 overlapping  
 those of \*\*\*IL\*\*\* . \*\*\*\*\*) . B chronic lymphocytic  
 leukemia (B-CLL)  
 is characterized by the accumulation of slow-dividing and  
 long-lived  
 monoclonal B cells, arrested at the intermediate stage of  
 their  
 differentiation. In vitro, B-CLL cells exhibit a spontaneous  
 apoptosis  
 regulated by different cytokines. In this report, we show that  
 IL-13 (10  
 to 200 ng/mL) acts directly on monoclonal B-CLL cells  
 from 12 patients.  
 (1) IL-13 enhances CD23 expression and induces soluble  
 CD23 secretion by  
 B-CLL cells but does not exhibit a growth factor activity. (2)  
 IL-13  
 inhibits IL-2 responsiveness of B-CLL cells, activated either  
 with IL-2  
 alone or through crosslinking of Igs or ligation of CD40  
 antigen. (3)  
 IL-13 protects B-CLL cells from in vitro spontaneous  
 apoptosis. The  
 effects of IL-13 on neoplastic B cells were slightly less than  
 those of  
 \*\*\*IL\*\*\* . \*\*\*\*\*) and occurred independently of the  
 presence of  
 \*\*\*IL\*\*\* . \*\*\*\*\*) . The present observations show  
 that IL-13 may  
 exhibit a negative regulatory effect on neoplastic B cells in  
 contrast with  
 that observed in normal B cells, and suggest that IL-13  
 could be an  
 important factor in the pathogenesis of CLL by preventing  
 the death of  
 monoclonal B cells. Moreover, B-CLL may be an interesting  
 model to study  
 the regulation of the expression of \*\*\*IL\*\*\* . \*\*\*\*\*)  
 \*\*\*receptor\*\*\* and/or signal transduction pathways.

L5 ANSWER 43 OF 82 MEDLINE  
 ACCESSION NUMBER: 96133964 MEDLINE  
 DOCUMENT NUMBER: 96133964  
 TITLE: Cloning and characterization of a binding  
 subunit of the  
 interleukin 13 receptor that is also a component of  
 the  
 interleukin 4 receptor.  
 AUTHOR: Hilton D J; Zhang J G; Metcalf D;  
 Alexander W S; Nicola N  
 A; Willson T A  
 CORPORATE SOURCE: Walter and Eliza Hall Institute of  
 Medical Research, Royal  
 Melbourne Hospital, Victoria, Australia.  
 CONTRACT NUMBER: CA-22556 (NCI)  
 SOURCE: PROCEEDINGS OF THE NATIONAL  
 ACADEMY OF SCIENCES OF THE  
 UNITED STATES OF AMERICA, (1996 Jan 9) 93  
 (1) 497-501.  
 Journal code: PV3. ISSN: 0027-8424.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 OTHER SOURCE: GENBANK-S80963  
 ENTRY MONTH: 199604  
 AB Interleukins 4 ( \*\*\*IL\*\*\* . \*\*\*\*\*) and 13 (IL-13)  
 have been found  
 previously to share receptor components on some cells, as  
 revealed by  
 receptor cross-competition studies. In the present study, the  
 cloning is  
 described of murine NR4, a previously unrecognized  
 receptor identified on  
 the basis of sequence similarity with members of the  
 hemopoietin receptor  
 family. mRNA encoding NR4 was found in a wide range of  
 murine cells and  
 tissues. By using transient expression in COS-7 cells, NR4  
 was found to  
 encode the \*\*\*IL\*\*\* . \*\*\*\*\*) \*\*\*receptor\*\*\*

alpha chain, a  
 low-affinity receptor capable of binding IL-13 but not  
 \*\*\*IL\*\*\* .  
 \*\*\*\*\*) or interleukins 2, -,7, -,9, or -15. Stable expression  
 of the  
 \*\*\*IL\*\*\* . \*\*\*\*\*) \*\*\*receptor\*\*\* alpha chain  
 (NR4) in CTL-2  
 cells resulted in the generation of high-affinity \*\*\*IL\*\*\* .  
 \*\*\*\*\*)  
 \*\*\*receptors\*\*\* capable of transducing a proliferative  
 signal in  
 response to IL-13 and, moreover, led to competitive  
 cross-reactivity in  
 the binding of \*\*\*IL\*\*\* . \*\*\*\*\*) and IL-13. These  
 results suggest  
 that the \*\*\*IL\*\*\* . \*\*\*\*\*) \*\*\*receptor\*\*\* alpha  
 chain (NR4) is  
 the primary binding subunit of the \*\*\*IL\*\*\* . \*\*\*\*\*)  
 \*\*\*receptor\*\*\* and may also be a component of  
 \*\*\*IL\*\*\* . \*\*\*\*\*)  
 receptors.

L5 ANSWER 44 OF 82 MEDLINE  
 ACCESSION NUMBER: 96082177 MEDLINE  
 DOCUMENT NUMBER: 96082177  
 TITLE: The insulin receptor substrate-1-related 4PS  
 substrate but  
 not the interleukin-2R gamma chain is involved in  
 interleukin-13-mediated signal transduction.  
 AUTHOR: Wang L M; Micheli P; Lie W R; Liu F; Lee  
 C C; Minty A; Sun  
 X J; Levine A; White M F; Pierce J H  
 CORPORATE SOURCE: Laboratory of Cellular and  
 Molecular Biology, National  
 Institutes of Health, Bethesda, MD 20892-4255,  
 USA.  
 SOURCE: BLOOD, (1995 Dec 1) 86 (11) 4218-27.  
 Journal code: A8G. ISSN: 0006-4971.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals;  
 Priority Journals; Cancer  
 Journals  
 ENTRY MONTH: 199603  
 AB Interleukin-13 (IL-13) induced a potent mitogenic  
 response in  
 IL-3-dependent TF-1 cells and DNA synthesis to a lesser  
 extent in MOTE and  
 FDC-P1 cells. IL-13 stimulation of these lines, like  
 \*\*\*IL\*\*\* .  
 \*\*\*\*\*) and insulin-like growth factor-1 (IGF-1),  
 resulted in tyrosine  
 phosphorylation of a 170-kD substrate. The  
 tyrosine-phosphorylated 170-kD  
 substrate strongly associated with the 85-kD subunit of  
 phosphoinositide-3  
 (PI-3) kinase and with Grb-2. Anti-4PS serum readily  
 detected the 170-kD  
 substrate in lysates from both TF-1 and FDC-P1 cells  
 stimulated with IL-13  
 or \*\*\*IL\*\*\* . \*\*\*\*\*) . These data provide evidence  
 that IL-13  
 induces tyrosine phosphorylation of the 4PS substrate,  
 providing an  
 essential interface between the \*\*\*IL\*\*\* . \*\*\*\*\*)  
 \*\*\*receptor\*\*\*  
 and signaling molecules containing SH2 domains. IL-13 and  
 \*\*\*IL\*\*\* .  
 \*\*\*\*\*) stimulation of murine L cell fibroblasts, which  
 endogenously  
 express the \*\*\*IL\*\*\* . \*\*\*\*\*) receptor (IL-4R alpha)  
 and lack  
 expression of the IL-2 receptor gamma subunit (IL-2R  
 gamma), resulted in  
 tyrosine phosphorylation of insulin receptor substrate-1  
 (IRS-1)/4PS.  
 Enhanced tyrosine phosphorylation of IRS-1/4PS was  
 observed in response to  
 \*\*\*IL\*\*\* . \*\*\*\*\*) , but not IL-13 treatment of L cells  
 transfected  
 with the IL-2R gamma chain. These results indicate that  
 IL-13 does not use  
 the IL-2R gamma subunit in its receptor complex and that  
 expression of  
 IL-2R gamma enhances, but is not absolutely required for  
 mediating  
 \*\*\*IL\*\*\* . \*\*\*\*\*) -induced tyrosine phosphorylation  
 of IRS-1/4PS.

L5 ANSWER 45 OF 82 MEDLINE  
 ACCESSION NUMBER: 96025882 MEDLINE  
 DOCUMENT NUMBER: 96025882  
 TITLE: \*\*\*IL\*\*\* . \*\*\*\*\*) induces germ-line IgE  
 heavy chain  
 gene transcription in human fetal pre-B cells.  
 Evidence for  
 differential expression of functional \*\*\*IL\*\*\* .  
 \*\*\*\*\*) and \*\*\*IL\*\*\* . \*\*\*\*\*)  
 \*\*\*receptors\*\*\*

during B cell ontogeny.

AUTHOR: Punnonen J; Cocks B G; de Vries J E  
CORPORATE SOURCE: DNAX Research Institute of Molecular and Cellular Biology, Human Immunology Department, Palo Alto, CA 94304, USA.  
SOURCE: JOURNAL OF IMMUNOLOGY, (1995 Nov 1) 155 (9) 4248-54.  
Journal code: IFB. ISSN: 0022-1767.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
ENTRY MONTH: 199602  
AB The present study demonstrates that \*\*\*IL\*\*\* - \*\*\*4\*\*\* induces germ-line IgE heavy chain (epsilon) gene transcription in human fetal splenic mononuclear cells; fetal bone marrow cells; highly purified sorted surface (s) mu+, CD10+, CD19+ immature B cells; and s mu-, cytoplasmic mu+, CD10+, CD19+ pre-B cells derived from human fetal bone marrow.  
Similar to observations in normal adult B cells, TGF-beta and IFN-gamma inhibited \*\*\*IL\*\*\* - \*\*\*4\*\*\* -induced germ-line epsilon RNA synthesis in fetal pre-B cells, whereas anti-CD40 mAbs and TNF-alpha had enhancing effects, suggesting that the general mechanisms regulating germ-line epsilon transcription in adult B cells and pre-B cells are similar. IL-13 also induced germ-line epsilon RNA synthesis in s mu+, CD10+, CD19+ immature B cells, but the level of transcription induced by IL-13 was significantly less than that induced by \*\*\*IL\*\*\* - \*\*\*4\*\*\*.  
Anti-CD40 mAbs strongly synergized with both \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 in inducing germ-line epsilon RNA synthesis by fetal immature B cells. Interestingly, IL-13 failed to induce germ-line epsilon RNA synthesis in s mu- pre-B cells even in the presence of anti-CD40 mAbs.  
These distinct effects of \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 suggest that functional IL-13R are expressed at a later stage of B cell ontogeny than IL-4R, and that IL-13, in contrast to \*\*\*IL\*\*\* - \*\*\*4\*\*\*, does not regulate pre-B cell differentiation. Given the fact that \*\*\*IL\*\*\* - \*\*\*4\*\*\* production appears to be enhanced in atopic individuals, the capacity of \*\*\*IL\*\*\* - \*\*\*4\*\*\* to induce germ-line epsilon transcription in human fetal immature B cells and pre-B cells suggests that commitment of B cell precursors to IgE-producing cells may occur during intrauterine life and may explain the increased IgE production in neonates with a family history of atopy.

L5 ANSWER 46 OF 82 MEDLINE  
ACCESSION NUMBER: 96025871 MEDLINE  
DOCUMENT NUMBER: 96025871  
TITLE: \*\*\*IL\*\*\* - \*\*\*4\*\*\* induces human B cell maturation and IgE synthesis in SCID-hu mice. Inhibition of ongoing IgE production by in vivo treatment with an \*\*\*IL\*\*\* - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* antagonist.  
AUTHOR: Carballido J M; Schols D; Namikawa R; Zurawski S; Zurawski G; Roncarolo M G; de Vries J E  
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute, Palo Alto, CA 94304, USA.  
SOURCE: JOURNAL OF IMMUNOLOGY, (1995 Nov 1) 155 (9) 4162-70.  
Journal code: IFB. ISSN: 0022-1767.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
ENTRY MONTH: 199602  
AB The effect of cytokine treatment on the in vivo maturation and Ig isotype

switching of human B cells was studied in a modified SCID-hu mouse model.  
SCID mice, subcutaneously cotransplanted with small fragments of fetal human thymus and bone (SCID-hu BM/T mice) generated all human leukocyte lineages including T and B lymphocytes, macrophages, and granulocytes. All SCID-hu BM/T mice spontaneously produced human IgM and IgG, whereas IgE and IgA were detected in 37 and 80% of the mice, respectively, indicating that productive human T-B cell interactions resulting in Ig isotype switching occur in these mice. Administration of \*\*\*IL\*\*\* - \*\*\*4\*\*\* to SCID-hu BM/T mice enhanced human B cell maturation, as judged by the increase in the percentages of CD45+, CD19+ bone marrow B cells expressing CD20, CD23, CD40, sIgM, and sIgD. Furthermore, these cells were also functionally more mature because they spontaneously produced human IgG/IgG4 in vitro and could be induced to secrete human IgE by addition of anti-CD40 mAb alone. In contrast, B cells isolated from PBS-treated mice only produced significant Ig levels after stimulation with anti-CD40 mAb in the presence of exogenous \*\*\*IL\*\*\* - \*\*\*4\*\*\*.  
\*\*\*IL\*\*\* - \*\*\*4\*\*\* administration also induced human IgE synthesis in 44% of the mice, which had no serum IgE before treatment. More importantly, ongoing human IgE synthesis in SCID-hu BM/T mice was suppressed by > 90% following administration of an \*\*\*IL\*\*\* - \*\*\*4\*\*\* mutant protein, which acts as an \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* antagonist. These results suggest that \*\*\*IL\*\*\* - \*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* antagonists have potential clinical utility in treating human atopic diseases associated with enhanced IgE production.

L5 ANSWER 47 OF 82 MEDLINE  
ACCESSION NUMBER: 95339858 MEDLINE  
DOCUMENT NUMBER: 95339858  
TITLE: Involvement of interleukin (IL)-13, but not \*\*\*IL\*\*\* - \*\*\*4\*\*\*, in spontaneous IgE and IgG4 production in nephrotic syndrome.  
AUTHOR: Kimata H; Fujimoto M; Furusho K  
CORPORATE SOURCE: Department of Pediatrics, Kyoto University Hospital, Japan.  
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 Jun) 25 (6) 1497-501.  
Journal code: EN5. ISSN: 0014-2980.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Cancer Journals  
ENTRY MONTH: 199510  
AB Nephrotic syndrome (NS) is a renal disease characterized by proteinuria and hypoalbuminemia. In NS patients without any allergic disease, serum IgE and IgG4 levels were selectively increased, and peripheral blood mononuclear cells (MNC) spontaneously produced IgE and IgG4. T cells produced interleukin (IL)-13 spontaneously, and B cells constitutively expressed \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\* (IL-13R). In addition, T cells stimulated surface IgE-negative (sIgE-) and sIgG4- B cells to produce IgE and IgG4, respectively, and IgE and IgG4 production was specifically blocked by anti-IL-13 antibody (Ab). MNC from atopic dermatitis (AD) patients also produced IgE and IgG4 spontaneously. However, in AD patients, T cells spontaneously produced \*\*\*IL\*\*\* - \*\*\*4\*\*\*, but not IL-13, and B cells constitutively expressed IL-4R, but not IL-13R. T cells stimulated sIgE- and sIgG4- B cells to produce IgE and IgG4, respectively, and the production was specifically blocked by anti-\*\*\*IL\*\*\* - \*\*\*4\*\*\* Ab. On the other hand, sIgE+ and

sIgG4+ B cells from both NS and AD patients spontaneously produced IgE and IgG4, respectively, and this production was not affected by T cells, anti-\*\*\*IL\*\*\* - \*\*\*4\*\*\* Ab, or anti-IL-13 Ab. These results indicate that IL-13 is involved in the enhanced production of IgE and IgG4 in NS, while \*\*\*IL\*\*\* - \*\*\*4\*\*\* is involved in these responses in AD.  
L5 ANSWER 48 OF 82 MEDLINE  
ACCESSION NUMBER: 95337763 MEDLINE  
DOCUMENT NUMBER: 95337763  
TITLE: Inhibition of human IgE synthesis in vitro and in SCID-hu mice by an interleukin-4 receptor antagonist.  
AUTHOR: Carballido J M; Aversa G; Schols D; Punnonen J; de Vries J E  
CORPORATE SOURCE: Human Immunology Department, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104, USA.  
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1995 May-Jun) 107 (1-3) 304-7.  
Journal code: BJ7. ISSN: 1018-2438.  
PUB. COUNTRY: Switzerland  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199510  
AB In the present study, it is shown that a human interleukin (\*\*\*IL\*\*\* - \*\*\*4\*\*\*) mutant protein (\*\*\*IL\*\*\* - \*\*\*4\*\*\* . Y124D) acts as a potent \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* antagonist. Human (h) \*\*\*IL\*\*\* - \*\*\*4\*\*\* . Y124D efficiently inhibits both \*\*\*IL\*\*\* - \*\*\*4\*\*\* - and IL-13-induced IgE production in vitro. In addition, hIL-4.Y124D strongly inhibits ongoing human IgE synthesis in SCID-hu mice. These inhibitory effects are specific, since human IgG levels were not significantly affected. These results confirm the notion that the \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* share a common component, which is required for signal transduction. In addition, they show that relatively large antagonistic polypeptides, such as hIL-4.Y124D have potential clinical utility in reducing IgE-mediated allergic diseases.  
L5 ANSWER 49 OF 82 MEDLINE  
ACCESSION NUMBER: 95325632 MEDLINE  
DOCUMENT NUMBER: 95325632  
TITLE: The IL-2 receptor gamma c chain does not function as a subunit shared by the \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\*. Implication for the structure of the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor.  
AUTHOR: He Y W; Malek T R  
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33136, USA.  
CONTRACT NUMBER: 1R01-CA45957 (NCI)  
SOURCE: JOURNAL OF IMMUNOLOGY, (1995 Jul 1) 155 (1) 9-12.  
Journal code: IFB. ISSN: 0022-1767.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
ENTRY MONTH: 199510  
AB The IL-2 receptor (IL-2R) gamma c subunit is also a component of the receptors for \*\*\*IL\*\*\* - \*\*\*4\*\*\*, IL-7, IL-9, and IL-15. The IL-4R and IL-13R appear to share a common subunit, and gamma c was proposed to be this shared subunit. In this study, we have assessed the relative contribution of gamma c to the mouse IL-4R and IL-13R. The MC/9 mast cell line constitutively expresses gamma c and proliferates to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13, but only the response to \*\*\*IL\*\*\* - \*\*\*4\*\*\* was

blocked by anti-gamma c mAbs. After transfection of the \*\*\*IL\*\*\* -  
 \*\*\*4\*\*\* - and IL-13-responsive gamma c-negative B9 plasmacytoma with full length (m gamma) or cytoplasmic-tailless gamma c cDNA (m gamma t), only the proliferative response to \*\*\*IL\*\*\* - \*\*\*4\*\*\* was affected by the surface expression of these gamma c molecules. The inability of m gamma or m gamma t expression to affect IL-13-induced proliferation by B9 indicates that gamma c does not obviously contribute to the IL-13R and does not function as the shared subunit of the IL-4R and IL-13R. This study suggests that there are two distinct IL-4R, one of which is independent of gamma c.

L5 ANSWER 50 OF 82 MEDLINE  
 ACCESSION NUMBER: 95263584 MEDLINE  
 DOCUMENT NUMBER: 95263584  
 TITLE: Interleukin-13 signal transduction in lymphohemopoietic cells. Similarities and differences in signal transduction with interleukin-4 and insulin.  
 AUTHOR: Welham M J; Leamonth L; Bone H; Schrader J W  
 CORPORATE SOURCE: Biomedical Research Centre, University of British Columbia, Vancouver, Canada.  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 May 19) 270 (20) 12286-96.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199508  
 AB Interleukin-13 (IL-13) and interleukin-4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) are related in structure and function and are thought to share a common receptor component. We have investigated the signal transduction pathways activated by these two growth factors, as well as insulin, in cell-lines and primary cells of lymphohemopoietic origin. All three factors induced the tyrosine phosphorylation of a protein of 170 kDa (p170), which coimmunoprecipitated with the p85 subunit of P13'-kinase, via high affinity interactions mediated by the SH2 domains of p85. Antibodies raised against the entire insulin-receptor substrate-1 (IRS-1) protein immunoprecipitated p170 much less efficiently than they did IRS-1 from 3T3 cells. However, antibodies directed against the conserved pleckstrin homology domain of IRS-1 immunoprecipitated both p170 and IRS-1 with similar efficiency, suggesting they share structural similarities in this region. In lymphohemopoietic cells, IL-13, \*\*\*IL\*\*\* - \*\*\*4\*\*\* , and insulin failed to induce increased tyrosine phosphorylation of Shc, or its association with grb2, modification of Sos1, or activation of erk-1 and erk-2 mitogen-activated protein kinases, suggesting that p170 mediates downstream pathways distinct from those mediated by IRS-1. Both IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* induced low levels of tyrosine phosphorylation of Tyk-2 and Jak-1. \*\*\*IL\*\*\* - \*\*\*4\*\*\* also activated the Jak-3-kinase, but, despite other similarities, IL-13 did not. Insulin failed to activate any of the known members of the Janus family of kinases. In that Jak-3 is reported to associate with the IL-2 gamma c chain, these data suggest that the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* does not utilize this subunit. However, both IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* induced tyrosine phosphorylation of the \*\*\*IL\*\*\* - \*\*\*4\*\*\* -140 kDa receptor chain, suggesting that this is a component of both receptors in these cells and accounts for the similarities in signaling pathways shared by IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* .

L5 ANSWER 51 OF 82 MEDLINE  
 ACCESSION NUMBER: 95238374 MEDLINE  
 DOCUMENT NUMBER: 95238374  
 TITLE: Receptor for interleukin 13. Interaction with interleukin 4 by a mechanism that does not involve the common gamma chain shared by receptors for interleukins 2, 4, 7, 9, and 15.  
 AUTHOR: Obiri N I; Debinski W; Leonard W J; Puri R K  
 CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Food and Drug Administration, Bethesda, Maryland 20892, USA.  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Apr 14) 270 (15) 8797-804.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199507  
 AB Interleukin 13 (IL-13) shares many biological properties with \*\*\*IL\*\*\* - \*\*\*4\*\*\* , and although the receptor for \*\*\*IL\*\*\* - \*\*\*4\*\*\* (IL-4R) has been characterized, the expression and structure of \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* are unknown. We report here that human renal cell carcinoma (RCC) cells express large numbers of functional IL-13R. Human B lymphocytes and monocytes expressed a very small number of IL-13R, while resting or activated human T cells expressed little or no IL-13R. \*\*\*IL\*\*\* - \*\*\*4\*\*\* did not compete for IL-13 binding, while IL-13 competed for \*\*\*IL\*\*\* - \*\*\*4\*\*\* binding, even though IL-4R and IL-13R are structurally distinct on human RCC cells. IL-13 cross-linked with one major protein that is similar in size to the gamma c subunit of IL-2, -4, -7, -9, and -15 receptors but was not recognized by anti-gamma c or anti-IL-4R antibodies. \*\*\*IL\*\*\* - \*\*\*4\*\*\* , on the other hand, cross-linked with two major proteins, the smaller of which appears to be similar in size to IL-13R and gamma c, but (like the IL-13R) it did not react with anti-gamma c antibody. Although as shown in this study and in previous studies, gamma c is a functional component of IL-4R in lymphoid cells, it does not appear to be associated with IL-4R on RCC cells. Even in the absence of common gamma chain \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 were able to up-regulate intracellular adhesion molecule-1 antigen on RCC cells. These data suggest that the interaction of IL-13 with IL-4R does not involve gamma c and IL-13R itself may be a novel subunit of the IL-4R.

L5 ANSWER 52 OF 82 MEDLINE  
 ACCESSION NUMBER: 95188408 MEDLINE  
 DOCUMENT NUMBER: 95188408  
 TITLE: Regulatory effects of IL-13 on synovial fluid macrophages and blood monocytes from patients with inflammatory arthritis.  
 AUTHOR: Hart P H; Ahern M J; Smith M D; Finlay-Jones J J  
 CORPORATE SOURCE: Department of Microbiology and Infectious Diseases, School of Medicine, Flinders University of South Australia, Adelaide.  
 SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 Mar) 99 (3) 331-7.  
 Journal code: DD7. ISSN: 0009-9104.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199506  
 AB Activated macrophages are central to the destructive processes of chronic inflammatory arthritis. In this study, it was hypothesized that IL-13, a product predominantly of 'Th2-type' lymphocytes, may be used therapeutically to down-regulate monocyte/macrophage activities at sites

of chronic inflammation. Synovial fluid mononuclear cells were isolated from 12 patients with chronic inflammatory arthritis. Peripheral blood mononuclear cells (PBMC) were isolated at the same time as synovial fluid cells from all 12 patients. IL-13 significantly inhibited lipopolysaccharide (LPS)-induced tumour necrosis factor-alpha (TNF-alpha) production by mononuclear cells from peripheral blood, but not synovial fluid. In contrast, IL-13 inhibited LPS-induced IL-1 beta production by all cells, and as a positive response to IL-13, CD23 expression was increased on both cell populations. Blood monocytes cultured for 7 days with granulocyte-macrophage colony-stimulating factor (GM-CSF) or M-CSF responded to IL-13 in a manner similar to that detected for synovial fluid-derived cells, with suppression of LPS-induced IL-1 beta, but not TNF-alpha, production. In all experiments, the responses to IL-13 were very similar to those detected to \*\*\*IL\*\*\* - \*\*\*4\*\*\* , but differed from those measured with IL-10. Thus, the responses to IL-13 by synovial fluid cells and cultured monocytes are not equal to those of blood monocytes. The similar responses to \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 support claims of a common element for signalling from the \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptors\*\*\*. Furthermore, the activity of a common receptor chain may be altered by monocyte activation and differentiation.

L5 ANSWER 53 OF 82 MEDLINE  
 ACCESSION NUMBER: 95181299 MEDLINE  
 DOCUMENT NUMBER: 95181299  
 TITLE: Characterization and comparison of the interleukin 13 receptor with the interleukin 4 receptor on several cell types.  
 AUTHOR: Vita N; Lefort S; Laurent P; Caput D; Ferrara P  
 CORPORATE SOURCE: Sanofi Recherche, Lab'ège, France.  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Feb 24) 270 (8) 3512-7.  
 Journal code: HIV. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals; Cancer Journals  
 ENTRY MONTH: 199506  
 AB We describe here the characterization of the interleukin ( \*\*\*IL\*\*\* ) \*\*\*13\*\*\* \*\*\*receptor\*\*\* and a comparison with the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor on different cell types. Several, but not all, of the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor-positive cells showed specific IL-13 binding, which was always completely displaced by \*\*\*IL\*\*\* - \*\*\*4\*\*\* . In the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* -positive cells, the IL-13 either completely or partially displaced the labeled \*\*\*IL\*\*\* . Further characterization of the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* in two cell lines, COS-3 and A431, representative of the groups of complete and partial displacement of \*\*\*IL\*\*\* - \*\*\*4\*\*\* by IL-13, respectively, showed that the IL-13 binds with high affinity (Kd approximately 300 pM) to both cells and that the number of binding sites is, in COS-3 cells, equivalent to that for \*\*\*IL\*\*\* - \*\*\*4\*\*\* and, in A431 cells, is smaller than that for \*\*\*IL\*\*\* . Cross-linking of labeled IL-13 yielded, on COS-3 cells, two affinity-labeled complexes of 220 and 70 kDa, and on A431 cells, one complex of 70 kDa; labeled \*\*\*IL\*\*\* - \*\*\*4\*\*\* yielded on both cells the same pattern of three complexes of 220, 145, and 70 kDa. Altogether, these results suggest that the \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* may be constituted by a subset of the \*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor

complex associated with at least one additional protein.

L5 ANSWER 54 OF 82 MEDLINE

ACCESSION NUMBER: 95137668 MEDLINE

DOCUMENT NUMBER: 95137668

TITLE: IL-13 has only a subset of \*\*\*IL\*\*\* -

\*\*\*4\*\*\* -like activities on B chronic lymphocytic leukaemia cells.

AUTHOR: Fluckiger A C; Briere F; Zurawski G; Bridon J M;

Banchereau J  
CORPORATE SOURCE: Schering-Plough, Laboratory for Immunological Research,  
Dardilly, France..

SOURCE: IMMUNOLOGY, (1994 Nov) 83 (3)  
397-403.

Journal code: GH7. ISSN: 0019-2805.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199505

AB The recently described interleukin-13 (IL-13) has been shown to share many of the effects of \*\*\*IL\*\*\* - \*\*\*4\*\*\* on normal B cells, including growth-promoting activity and induction of CD23. In this study, we

compared the effects of IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* on B chronic lymphocytic leukaemias (B-CLL) cells. After anti-CD40 activation, both

IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* promoted the DNA synthesis of B-CLL cells and increased the recovery of viable cells. The time kinetics of the

proliferative response of B-CLL cells to IL-13 or \*\*\*IL\*\*\* - \*\*\*4\*\*\* were superimposable and showed the long-lasting effect of both cytokines.

As on normal B cells, both \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 synergized with IL-10 to enhance B-CLL DNA synthesis. Moreover, IL-13, like

\*\*\*IL\*\*\* - \*\*\*4\*\*\*, was able to increase CD23 expression on anti-CD40-activated leukaemic B cells. The CD23 up-regulation and the DNA

synthesis induced by IL-13 on anti-CD40-activated B-CLL cells, were significantly reduced when B-CLL cells were cultured with anti-\*\*\*IL\*\*\*

- \*\*\*4\*\*\* receptor monoclonal antibody, suggesting a common pathway for IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* signalling. However, after

cross-linking of surface IgM, \*\*\*IL\*\*\* - \*\*\*4\*\*\* strongly inhibited the IL-2-induced DNA synthesis of B-CLL cells, whereas IL-13 did not

inhibit IL-2-driven proliferation of anti-IgM-activated B-CLL cells. Furthermore, while \*\*\*IL\*\*\* - \*\*\*4\*\*\* strongly up-regulated the

expression of CD23 on anti-IgM-activated leukaemic B cells, IL-13 only marginally increased it. Finally, IL-13, in contrast to \*\*\*IL\*\*\* -

\*\*\*4\*\*\*, did not prevent the entry of B-CLL cells into apoptosis. Thus

IL-13 and \*\*\*IL\*\*\* - \*\*\*4\*\*\* display comparable effects on anti-CD40-activated B-CLL cells, which are blocked by anti-\*\*\*IL\*\*\*

- \*\*\*4\*\*\* receptor (IL-4R) monoclonal antibodies. However, IL-13-dependent effects are absent or inefficient in non-activated or anti-IgM-activated

B-CLL cells. This suggests that such cells may lack functional \*\*\*IL\*\*\*

- \*\*\*13\*\*\* \*\*receptors\*\*\*, though IL-13R and IL-4R on B-CLL cells

share a common component.

L5 ANSWER 55 OF 82 MEDLINE

ACCESSION NUMBER: 94065589 MEDLINE

DOCUMENT NUMBER: 94065589

TITLE: An interleukin 4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* )

mutant protein inhibits both \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13-induced

human immunoglobulin G4 (IgG4) and IgE synthesis and B cell

proliferation: support for a common component shared by \*\*\*IL\*\*\* - \*\*\*4\*\*\* and \*\*\*IL\*\*\* -

\*\*\*13\*\*\* \*\*receptors\*\*\*.

AUTHOR: Aversa G; Punnnonen J; Cocks B G; de Waal

Malefyt R; Vega F

Jr; Zurawski S M; Zurawski G; de Vries J E

CORPORATE SOURCE: Human Immunology Department, DNAX Research Institute, Palo Alto, California 94304-1104.

SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Dec 1) 178 (6)

2213-8.  
Journal code: I2V. ISSN: 0022-1007.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199403

AB Interleukin 4 ( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) and IL-13 share many biological functions. Both cytokines promote growth of activated human B cells and

induce naive human surface immunoglobulin D+ (sIgD+) B cells to produce

IgG4 and IgE. Here we show that a mutant form of human \*\*\*IL\*\*\* -

\*\*\*4\*\*\*, in which the tyrosine residue at position 124 is replaced by

aspartic acid (hIL-4.Y124D), specifically blocks \*\*\*IL\*\*\* - \*\*\*4\*\*\*

and IL-13-induced proliferation of B cells costimulated by anti-CD40 mAbs

in a dose-dependent fashion. A mouse mutant \*\*\*IL\*\*\* - \*\*\*4\*\*\*

protein (mIL-4.Y119D), which antagonizes the biological activity of mouse

\*\*\*IL\*\*\* - \*\*\*4\*\*\*, was ineffective. In addition, hIL-4.Y124D, at

concentrations of up to 40 nM, did not affect IL-2-induced B cell

proliferation. hIL-4.Y124D did not have detectable agonistic activity in

these B cell proliferation assays. Interestingly, hIL-4.Y124D also

strongly inhibited both \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13-induced IgG4 and

IgE synthesis in cultures of peripheral blood mononuclear cells, or highly

purified sIgD+ B cells cultured in the presence of anti-CD40 mAbs.

\*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13-induced IgE responses were inhibited >

95% at an approximately 50- or approximately 20-fold excess of hIL-4.Y124D,

respectively, despite the fact that the \*\*\*IL\*\*\* - \*\*\*4\*\*\* mutant

protein had a weak agonistic activity. This agonistic activity was 1.6 +/-

1.9% (n = 4) of the maximal IgE responses induced by saturating

concentrations of \*\*\*IL\*\*\* - \*\*\*4\*\*\*. Taken together, these data

indicate that there are commonalities between the \*\*\*IL\*\*\* - \*\*\*4\*\*\*

and \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*receptor\*\*\*. In addition, since

hIL-4.Y124D inhibited both \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13-induced IgE

synthesis, it is likely that antagonistic mutant \*\*\*IL\*\*\* - \*\*\*4\*\*\*

proteins may have potential clinical use in the treatment of IgE-mediated

allergic diseases.

L5 ANSWER 56 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 2000:104883 BIOSIS

DOCUMENT NUMBER: PREV200000104883

TITLE: Functional implications for signaling via the IL4R/IL13R

complex on bovine cells.

AUTHOR(S): Trigona, Wendy L.; Brown, Wendy C.;

Estes, D. Mark (1)

CORPORATE SOURCE: (1) College of Veterinary Medicine, Department of

Veterinary Pathobiology, University of Missouri, Columbia,

MO, 65211 USA

SOURCE: Veterinary Immunology and Immunopathology, (Dec. 15, 1999)

Vol. 72, No. 1-2, pp. 73-79.

ISSN: 0165-2427.

DOCUMENT TYPE: General Review

LANGUAGE: English

SUMMARY LANGUAGE: English

AB \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 share a wide range of activities on

monocytes, epithelial cells and B cells and thus play an important role in

host defense. Many of these activities are not conserved among species as

human, but not murine, B cells are thought to be responsive to IL-13. We

previously demonstrated that human IL-13 is highly conserved at the

nucleic acid level with a candidate bovine IL-13 cDNA

homologue. Moreover,

recombinant human IL-13 stimulates Ig secretion by

appropriately activated bovine B cells. These studies have been extended to

examining Ig class switching at both the protein and mRNA levels in addition

to examining other markers of cellular activation. Our results suggest that

IL-13 influences B cell differentiation by enhancing IgM, IgG1, and IgE

production. IL-13 stimulation alone increases MHC class II expression and

progression through cell cycle, although at lower levels in comparison to

rbolL-4. The biology of the receptors for \*\*\*IL\*\*\* - \*\*\*4\*\*\* and

IL-13 is complex and raises several key questions with regard to

\*\*\*IL\*\*\* - \*\*\*4\*\*\* -dependent and -independent mechanisms of host

immunomodulation. Recent studies suggest that at least four chains are

involved. These include the p140 \*\*\*IL\*\*\* - \*\*\*4\*\*\* binding chain

(IL-4Ralpha), the common gamma chain (gammac chain), \*\*\*IL\*\*\* -

\*\*\*13\*\*\* \*\*receptor\*\*\* alpha-1 chain (IL-13Ralpha-1) and the

\*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*receptor\*\*\* alpha-2 chain (IL-13Ralpha-2).

We have recently cloned cDNAs for the bovine homologues of the

IL-13Ralpha-1 and IL-4Ralpha chains and evaluated mRNA expression for a

variety of cell types following stimulation. The expression patterns and

their implications for receptor chain utilization in signaling via these

key TH2 signature cytokines will be discussed.

L5 ANSWER 57 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1999:464170 BIOSIS

DOCUMENT NUMBER: PREV199900464170

TITLE: A key role for interleukin-13 in allergic asthma. AUTHOR(S): Minty, Adrian (1)

CORPORATE SOURCE: (1) Sanofi Synthelabo Recherche, 31676, Labège France

SOURCE: M-S (Medicine Sciences), (June July, 1999) Vol. 15, No.

6-7, pp. 863-867.

ISSN: 0767-0974.

DOCUMENT TYPE: Article

LANGUAGE: French

L5 ANSWER 58 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1999:314766 BIOSIS

DOCUMENT NUMBER: PREV199900314766

TITLE: Molecular regulation of human IgE synthesis. AUTHOR(S): Yanagihara, Yukiyoshi (1)

CORPORATE SOURCE: (1) Clinical Research Center for Allergy, National

Sagamihara Hospital, 18-1 Sakuradai, Sagami-hara, 228-8522

Japan

SOURCE: Allergy International, (June, 1999) Vol. 48, No. 2, pp.

111-119.

ISSN: 1323-8930.

DOCUMENT TYPE: General Review

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Human IgE synthesis is largely dependent on the production of interleukin

( \*\*\*IL\*\*\* - \*\*\*4\*\*\* ) or IL-13 and the expression of CD40 ligand.

Such B cell help is not only provided by CD4+ T cells, but also by CD8+ T

cells, gamma delta T cells, mast cells, basophils and eosinophils. The

\*\*\*IL\*\*\* - \*\*\*4\*\*\* receptor alpha chain (IL-4Ralpha) expressed on B

cells is shared by the functional IL-4R and IL-13R and is a crucial

component required for signal transduction leading to germline Cepsilon

transcription, which is a prerequisite for IgE isotype switching.

Interleukin-4 activates Janus kinase (JAK)1, JAK3 and phosphatidylinositol

3-kinase (PI3-K) and, subsequently, induces nuclear translocation of

signal transducers and activators of transcription (STAT)6 and nuclear

factor (NF)-kappaB, which interact at the level of the Iepsilon promoter.

The two variants of the IL-4Ralpha, which have been identified in

association with atopy, are associated with enhanced



responsiveness to  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* . Ligation of CD40 on B cells  
 up-regulates  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* - or IL-13-driven germline Cepsilon  
 transcription  
 and further induces deletional switch recombination that  
 results in IgE  
 isotype switching, mature Cepsilon transcription and IgE  
 synthesis.  
 Signaling pathways mediated by CD40 include activation of  
 Lyn, PI3-K, JAK3  
 and members of the mitogen-activated protein kinase  
 subfamily,  
 multimerization of tumor necrosis factor-alpha  
 receptor-associated factor  
 (TRAF)2, TRAF3, TRAF5 and TRAF6 and translocation of  
 NF-kappaB and STAT3.  
 In addition, Ku70/86, DNA-dependent protein kinase and  
 rad51/54 may be  
 involved in switch recombination. Taken together, activation  
 of kinases,  
 induction of second messengers, nuclear expression of  
 transcription  
 factors and localization of DNA-binding proteins are  
 integrated to produce  
 the terminal differentiation of a B cell into an IgE-secreting  
 plasma  
 cell. Elucidation of the detailed mechanisms of IgE isotype  
 switching will  
 contribute to the development of potential new therapeutic  
 procedures for  
 the regulation of the IgE response in atopic patients.

L5 ANSWER 59 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1999:289383 BIOSIS  
 DOCUMENT NUMBER: PREV199900289383  
 TITLE: Interleukin-13 enhances pancreatic cancer cell  
 growth via  
 mitogen-activated protein kinase: Evidence for  
 autocrine  
 actions.  
 AUTHOR(S): Kommunn, Marko (1); Joerg, Kleeff (1);  
 Beger, H. G.; Korc,  
 Murray  
 CORPORATE SOURCE: (1) Univ of CA, Irvine, Irvine, CA  
 USA  
 SOURCE: Gastroenterology, (April, 1999) Vol. 116,  
 No. 4 PART 2, pp.  
 A442.  
 Meeting Info.: Digestive Disease Week and the  
 100th Annual  
 Meeting of the American Gastroenterological  
 Association  
 Orlando, Florida, USA May 16-19, 1999 American  
 Gastroenterological Association  
 ISSN: 0016-5085.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 60 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1999:287888 BIOSIS  
 DOCUMENT NUMBER: PREV199900287888  
 TITLE: Distinct signaling pathways triggered by  
 \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\* - and \*\*\*IL\*\*\* - \*\*\*13\*\*\* .  
 \*\*\*receptor\*\*\*  
 complexes.  
 AUTHOR(S): Friedrich, Karlheinz (1); Brundlein,  
 Stephanie (1);  
 Kammer, Winfried (1); Lischke, Antje (1); Erhardt,  
 Ingrid  
 (1)  
 CORPORATE SOURCE: (1) Physiologische Chemie II,  
 Biozentrum der Universitaet  
 Wuerzburg, Am Hubland, D-97074, Wuerzburg  
 Germany  
 SOURCE: European Journal of Cell Biology, (1999)  
 Vol. 78, No.  
 SUPPL. 49, pp. 67.  
 Meeting Info.: 23rd Annual Meeting of the German  
 Society  
 for Cell Biology Rostock, Germany March 14-18,  
 1999 German  
 Society for Cell Biology  
 ISSN: 0171-9335.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 61 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1998:463461 BIOSIS  
 DOCUMENT NUMBER: PREV199800463461  
 TITLE: \*\*\*IL4\*\*\* and IL13 bind to different types  
 of  
 functional \*\*\*IL4\*\*\* / \*\*\*IL13\*\*\*  
 \*\*\*receptors\*\*\*  
 on human lung fibroblasts.  
 AUTHOR(S): Doucet, C. (1); Brouty-Boye, D. (1);  
 Pottin-Clemenceau, C.  
 (1); Jasmin, C. (1); Canonica, G.; Azzarone, B. (1)  
 CORPORATE SOURCE: (1) U268 INSERM, 16 av. PV

Couturier, 94807 Villejuif Cedex  
 France  
 SOURCE: Research in Immunology, (March-April,  
 1998) Vol. 149, No.  
 3, pp. 268.  
 Meeting Info.: Meeting on New Therapeutic  
 Approaches for  
 Allergic Diseases of the Respiratory Tract Paris,  
 France  
 April 1-4, 1998  
 ISSN: 0923-2494.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 62 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1998:69478 BIOSIS  
 DOCUMENT NUMBER: PREV19980069478  
 TITLE: The \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* regulates  
 IL-13 and \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* activities.  
 AUTHOR(S): Orchansky, Patricia L.; Lee, Frances;  
 Schrader, John W.  
 CORPORATE SOURCE: Univ. B.C., Biomedical Res.  
 Centre, 2222 Health Sciences  
 Mall, Vancouver, BC V6T 1Z3 Canada  
 SOURCE: Cytokine, (Nov., 1997) Vol. 9, No. 11, pp.  
 932.  
 Meeting Info.: Fifth Annual Conference of the  
 International  
 Cytokine Society Lake Tahoe, Nevada, USA  
 November 9-13,  
 1997 International Cytokine Society  
 ISSN: 1043-4666.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 63 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1996:456265 BIOSIS  
 DOCUMENT NUMBER: PREV199699178621  
 TITLE: Modulation of the human IgE response.  
 AUTHOR(S): De Vries, J. E. (1); Yssel, H.  
 CORPORATE SOURCE: (1) DNAX Res. Inst., 901  
 California Avenue, Palo Alto, CA  
 94304 USA  
 SOURCE: European Respiratory Journal Supplement,  
 (1996) Vol. 9, No.  
 SUPPL. 22, pp. 58S-62S.  
 ISSN: 0904-1850.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 AB Studies on the immunological basis of allergic diseases  
 have indicated  
 that enhanced production of the cytokines interleukin (   
 \*\*\*IL\*\*\* )-  
 \*\*\*\*4\*\*\* and IL-13 and the reduced production of  
 interferon-gamma  
 (IFN-gamma) by allergen-specific T-cells contribute to  
 enhanced  
 immunoglobulin E (IgE) synthesis and the development of  
 allergic disease  
 in certain individuals. Therefore, inhibition of \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\*  
 and IL-13 synthesis or blocking of activities of these  
 cytokines would be  
 one approach to inhibiting IgE production. In the present  
 communication,  
 novel approaches toward this goal are discussed. It is shown  
 that an  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* mutant protein, in which the  
 tyrosine residue at  
 position 124 is replaced by aspartic acid ( \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\*  
 .Y124D), binds with high affinity to the \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\*  
 receptor, without receptor activation. \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\* .Y124D acts  
 as a potent antagonist both of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and  
 IL-13 activity  
 in vitro, and inhibits immunoglobulin G-4 (IgG-4) and IgE  
 production  
 induced by these cytokines. These data are compatible with  
 the notion that  
 the \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptors\*\*\* are complex receptors, which share a  
 common component,  
 which is required for signal transduction. In addition, it has  
 been

demonstrated that allergen-specific T-cells, belonging to the  
 T-helper 2  
 (Th2) subset can be rendered anergic after incubation with  
 allergen-derived peptides representing minimal T-cell  
 activation inducing  
 epitopes. These anergic Th2 cells failed to produce  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*  
 and IL-13, and failed to proliferate after activation with  
 allergen and  
 antigen-presenting cells (APC). The anergized T cells also  
 failed to give  
 B-cells help in IgE synthesis, although they expressed  
 normal levels of

the CD40 ligand (CD40L). Exogenous \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\* or IL-13  
 failed to restore IgE synthesis, indicating that in addition to  
 CD40L  
 other co-stimulatory signals are required for productive  
 T-cell/B-cell  
 interactions, resulting in IgE synthesis. IgE production was  
 restored by  
 exogenous IL-2, demonstrating that IL-2 reverses the  
 nonresponsive state  
 and helper function of these nonresponsive T-cells. It is  
 tempting to  
 speculate that induction of T-cell nonresponsiveness by  
 allergen derived  
 peptides may represent the underlying mechanisms for  
 successful  
 immunotherapy in allergic patients.

L5 ANSWER 64 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1996:450919 BIOSIS  
 DOCUMENT NUMBER: PREV199699173275  
 TITLE: Stimulation of signal transduction pathways in  
 lymphocytes  
 from patients with X-SCID: Activation through the  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* but not the IL-2 receptor.  
 AUTHOR(S): Smith, Susan (1); Johnston, James; Jahn,  
 Thomas; Puck,  
 Jennifer; O'Shea, John; Weinberg, Kenneth;  
 Taylor, Naomi  
 CORPORATE SOURCE: (1) Div. Res. Immunol., Child.  
 Hosp. Los Angeles, Los  
 Angeles, CA USA  
 SOURCE: Experimental Hematology (Charlottesville),  
 (1996) Vol. 24,  
 No. 9, pp. 1100.  
 Meeting Info.: 25th Annual Meeting of the  
 International  
 Society for Experimental Hematology New York,  
 New York, USA  
 August 23-27, 1996  
 ISSN: 0301-472X.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 65 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1995:382536 BIOSIS  
 DOCUMENT NUMBER: PREV199598396836  
 TITLE: Modulation of human B cell maturation and  
 IgE synthesis by  
 \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and an \*\*\*IL\*\*\* -  
 \*\*\*\*4\*\*\* /  
 \*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\*  
 antagonist in  
 SCID-hu mice.  
 AUTHOR(S): Carballido, J. M.; Schols, D.; Namikawa,  
 R.; Roncarolo,  
 M.-G.; De Vries, J. E.  
 CORPORATE SOURCE: DNAX Res. Inst., Palo Alto, CA  
 USA  
 SOURCE: 9TH INTERNATIONAL CONGRESS OF  
 IMMUNOLOGY.. (1995) pp. 326.  
 The 9th International Congress of Immunology.  
 Publisher: 9th International Congress of  
 Immunology San  
 Francisco, California, USA.  
 Meeting Info.: Meeting Sponsored by the  
 American  
 Association of Immunologists and the  
 International Union of  
 Immunological Societies San Francisco, California,  
 USA July  
 23-29, 1995  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L5 ANSWER 66 OF 82 BIOSIS COPYRIGHT 2000 BIOSIS  
 ACCESSION NUMBER: 1994:139011 BIOSIS  
 DOCUMENT NUMBER: PREV199497152011  
 TITLE: IL-13-induced B cell proliferation and IgE  
 synthesis is  
 blocked by an \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* mutant  
 protein:  
 Support for a shared component of the \*\*\*IL\*\*\*  
 -  
 \*\*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
 \*\*\*receptors\*\*\*  
 AUTHOR(S): Aversa, Gregorio; Cocks, Benjamin;  
 Punnonen, Juha; De-Waal  
 Malefyt, Rene; Vega, Felix, Jr.; Zurawski, Sandra  
 M.;  
 Zurawski, Gerard; De Vries, Jan E.  
 CORPORATE SOURCE: Dep. Human Immunol., DNAX  
 Res. Inst. Mol. Cellular Biol.,  
 901 California Ave., Palo Alto, CA 94304 USA  
 SOURCE: Journal of Leukocyte Biology, (1993) Vol. 0,  
 No. SUPPL.,  
 pp. 93.  
 Meeting Info.: International Congress on the



Regulation of  
Leukocyte Production and Immune Function held  
at the Joint  
Meeting of the Australasian Society for  
Immunology and  
Society for Leukocyte Biology Sydney, New  
South Wales,  
Australia December 1-5, 1993  
ISSN: 0741-5400.  
DOCUMENT TYPE: Conference  
LANGUAGE: English

L5 ANSWER 67 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 2000:184125 SCISEARCH  
THE GENUINE ARTICLE: 289BV  
TITLE: Novel polymorphism in the coding region of  
the \*\*\*IL\*\*\*  
- \*\*\*13\*\*\* \*\*\*receptor\*\*\* alpha' gene:  
Association  
study with atopic asthma in the Japanese  
population  
AUTHOR: Ahmed S; Ihara K (Reprint); Sasaki Y;  
Nakao F; Nishima S;  
Fujino T; Hara T  
CORPORATE SOURCE: KYUSHU UNIV, GRAD SCH  
MED SCI, DEPT PEDIAT, HIGASHI KU,  
3-1-1 MAIDASHI, FUKUOKA 8128582, JAPAN  
(Reprint); KYUSHU  
UNIV, GRAD SCH MED SCI, DEPT PEDIAT,  
HIGASHI KU, FUKUOKA  
8128582, JAPAN; NATL MINAMI FUKUOKA  
CHEST HOSP, FUKUOKA,  
JAPAN; SHIN KOKURA HOSP, DIV PEDIAT,  
KITAKYUSHU, FUKUOKA,  
JAPAN  
COUNTRY OF AUTHOR: JAPAN  
SOURCE: EXPERIMENTAL AND CLINICAL  
IMMUNOGENETICS, (1 MAR 2000)  
Vol. 17, No. 1, pp. 18-22.  
Publisher: KARGER, ALLSCHWILERSTRASSE  
10, CH-4009 BASEL,  
SWITZERLAND.  
ISSN: 0254-9670.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 14  
\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*  
AB Interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* and IL-13 play  
key roles in the  
development of atopic asthma, The \*\*\*IL\*\*\* -  
\*\*\*13\*\*\*  
\*\*\*receptor\*\*\* (R) alpha' chain is a component of both  
IL-4R and IL-13R  
complexes. By screening the whole coding region of the  
IL-13R alpha' gene  
for polymorphisms, we identified a new polymorphism at  
nucleotide position  
1050 from the ATG start codon. The allelic frequency of the  
CT  
polymorphism in the Japanese population was found to be  
0.97:0.03. Because  
of the low frequency of the T allele, the association study  
failed to  
indicate any significant association between this  
polymorphism and atopic  
asthma in the Japanese population. Further studies are  
required in other  
racial groups with higher frequencies of this polymorphism  
to elucidate  
the association. Copyright (C) 2000 S. Karger AG, Basel.

L5 ANSWER 68 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 2000:734 SCISEARCH  
THE GENUINE ARTICLE: 266FD  
TITLE: Genetic and environmental interaction in  
allergy and  
asthma  
AUTHOR: Holgate S T (Reprint)  
CORPORATE SOURCE: SOUTHAMPTON GEN HOSP,  
RESP CELL & MOL BIOL DIV, LEVEL D,  
CTR BLOCK, SOUTHAMPTON SO16 6YD,  
HANTS, ENGLAND (Reprint)  
COUNTRY OF AUTHOR: ENGLAND  
SOURCE: JOURNAL OF ALLERGY AND  
CLINICAL IMMUNOLOGY, (DEC 1999)  
Vol. 104, No. 6, pp. 1139-1146.  
Publisher: MOSBY-YEAR BOOK INC, 11830  
WESTLINE INDUSTRIAL  
DR, ST LOUIS, MO 63146-3318.  
ISSN: 0091-6749.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE; CLIN  
LANGUAGE: English  
REFERENCE COUNT: 72  
\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*

AB Asthma is an inflammatory disorder of the airways  
involving coordinate  
up-regulation of T(H)2-type cytokines encoded in a cluster  
on chromosome  
5q(31-33) on T Cells and inflammatory cells. There is also a  
requirement  
for local airway susceptibility factors that, together with  
T(H)2  
polarization, results in hyperresponsiveness, variable airflow  
obstruction, and, over time, remodeling of the airway wall,  
Asthma has  
strong genetic and environmental components that interact  
both in the  
induction and subsequent expression of the disease  
phenotypes. Multiple  
genes are involved and probably interact. Whole genome  
screens are  
beginning to identify gene-rich regions of special relevance  
to asthma and  
atopy, although a novel disease-related gene has yet to be  
discovered from  
these. By contrast, there are a plethora of candidate genes  
whose function  
in relation to disease pathophysiologic mechanisms and  
response to  
treatment are known. Two examples are polymorphisms  
involving \*\*\*IL\*\*\*  
- \*\*\*4\*\*\* receptors and the enzymes controlling  
cysteinyl Leukotriene  
production. Abnormal signaling between the epithelium,  
which is in contact  
with the environment, and the underlying (mgo)fibroblasts  
and dendritic  
cells indicating reactivation of the epithelial mesenchymal  
trophic unit,  
which is involved in fetal lung development and branching,  
provide a basis  
for asthma that encapsulates both T(H)2 polarization and  
airway wall  
remodeling.

L5 ANSWER 69 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 1999:141499 SCISEARCH  
THE GENUINE ARTICLE: 165GT  
TITLE: Development of a recombinant  
interleukin-4-Pseudomonas  
exotoxin for therapy of glioblastoma  
AUTHOR: Puri R K (Reprint)  
CORPORATE SOURCE: NIH, LAB MOL TUMOR BIOL,  
DIV CELLULAR & GENE THERAPIES,  
CTR BIOL EVALUAT & RES, FOOD & DRUG  
ADM, BETHESDA, MD  
20892 (Reprint)  
COUNTRY OF AUTHOR: USA  
SOURCE: TOXICOLOGIC PATHOLOGY, (JAN-FEB  
1999) Vol. 27, No. 1, pp.  
53-57.  
Publisher: SOC TOXICOLOGIC  
PATHOLOGISTS, 1041 NEW  
HAMPSHIRE ST PO BOX 368, LAWRENCE,  
KS 66044.  
ISSN: 0192-6233.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 28

\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*  
AB About 12,000 Americans are diagnosed with malignant  
astrocytoma each  
year. Despite surgery, radiotherapy, and chemotherapy, the  
prognosis of  
these patients remains poor. Targeted toxins based on the  
identification  
of novel antigens or receptors provide a promising new  
approach to  
treating cancer. We have identified one such cell surface  
protein in the  
form of interleukin ( \*\*\*IL\*\*\* )- \*\*\*4\*\*\* receptors  
(IL-4R) on human  
malignant astrocytoma. Normal brain tissues from frontal  
cortex and  
temporal lobe cortex do not express IL-4R. To target IL-4R,  
we generated a  
chimeric fusion protein composed of \*\*\*IL\*\*\* -  
\*\*\*4\*\*\* and  
Pseudomonas exotoxin ( \*\*\*IL4\*\*\* -PE). This toxin is  
highly cytotoxic to  
IL-4R-bearing human brain cancer cells. Preclinical  
toxicologic  
experiments were performed in mice, rats, and guinea pigs  
to determine an  
maximum tolerated dose. Intrathecal administration in  
cynomolgus monkeys  
produced high cerebrospinal fluid levels without any central  
nervous  
system or other abnormalities. When \*\*\*IL4\*\*\* -PE was  
injected into the  
right frontal cortex of rats, localized necrosis was observed

at 1,000 but  
not less than or equal to 100 mu g/ml doses. Intravenous  
administration of  
this biologic to monkeys produced reversible grade 3 or  
grade 4 elevations  
of hepatic enzymes in a dose-dependent manner. These  
results indicate that  
localized administration can produce nontoxic levels of  
\*\*\*IL4\*\*\* -PE  
that may have significant activity against astrocytoma. In  
vivo  
experiments with nude mice have demonstrated that  
\*\*\*IL4\*\*\* -PE has  
significant antitumor activity against human glioblastoma  
tumor model.  
Intratumor administration of \*\*\*IL4\*\*\* -PE has been  
initiated for the  
treatment of malignant astrocytoma in a phase I clinical trial.

L5 ANSWER 70 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 1998:952058 SCISEARCH  
THE GENUINE ARTICLE: 146ZW  
TITLE: Comparative studies on the effects of  
interleukin-4 and  
interleukin-13 on cytokine and prostaglandin E-2  
production by amnion-derived WISH cells  
AUTHOR: Keelan J A (Reprint); Sato T A; Mitchell M  
D  
CORPORATE SOURCE: UNIV AUCKLAND, SCH MED,  
FAC MED & HLTH SCI, DEPT PHARMACOL  
& CLIN PHARMACOL, PRIVATE BAG 92019,  
AUCKLAND, NEW ZEALAND  
(Reprint)  
COUNTRY OF AUTHOR: NEW ZEALAND  
SOURCE: AMERICAN JOURNAL OF  
REPRODUCTIVE IMMUNOLOGY, (NOV 1998)  
Vol. 40, No. 5, pp. 332-338.  
Publisher: MUNKSGAARD INT PUBL LTD, 35  
NORRE SOGADE, PO  
BOX 2148, DK-1016 COPENHAGEN,  
DENMARK.  
ISSN: 8755-8920.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 39  
\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*  
AB PROBLEM: In hematopoietic cells, interleukin (IL)-13  
shares many  
actions with \*\*\*IL\*\*\* - \*\*\*4\*\*\* . The effects of IL-13  
in gestational  
tissues have yet to be reported, however. We compared the  
effects of  
\*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 on the production of  
cytokines and  
prostaglandin E-2 (PGE(2)) in epithelial amnion-derived  
WISH cells.  
METHOD OF STUDY: WISH cells were treated with  
\*\*\*IL\*\*\* - \*\*\*4\*\*\*  
or IL-13 (0.08-10 ng/ml) with/without cotreatment with IL-1  
beta (0.2  
ng/ml), tumor necrosis factor-alpha (10 ng/ml) or epidermal  
growth factor  
(5 ng/ml). The production of IL-6, IL-8, and PGE(2) was  
measured by  
immunoassay after 16 hr.  
RESULTS: Both \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13  
inhibited PGE(2)  
production with indistinguishable concentration-response  
curves, under  
basal or stimulated conditions. The maximal inhibition of 1  
beta-stimulated PGE(2) production (to 28% +/- 10% of  
control) was seen at  
10 ng/ml of \*\*\*IL\*\*\* - \*\*\*4\*\*\* or IL-13. Basal IL-6  
production was  
stimulated approximately twofold by \*\*\*IL\*\*\* -  
\*\*\*4\*\*\* and IL-13,  
whereas \*\*\*IL\*\*\* - \*\*\*4\*\*\* and IL-13 both inhibited  
cytokine-stimulated (but not basal) IL-8 production by  
approximately 50%.  
In the presence of 1 ng/ml of \*\*\*IL\*\*\* - \*\*\*4\*\*\* ,  
IL-13 was unable  
to further inhibit PGE(2) production.  
CONCLUSIONS: The inhibition of PGE(2) and IL-8  
production by \*\*\*IL\*\*\*  
- \*\*\*4\*\*\* in WISH cells is mimicked by IL-13. Both  
cytokines, probably  
through binding to a common receptor complex, may share  
a role in  
suppressing inflammatory reactions within intrauterine  
tissues.

L5 ANSWER 71 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 96:742819 SCISEARCH  
THE GENUINE ARTICLE: VL234  
TITLE: INTERLEUKIN-13 INHIBITS GROWTH OF  
HUMAN RENAL-CELL

CARCINOMA-CELLS INDEPENDENTLY OF  
THE P140 INTERLEUKIN-4  
RECEPTOR CHAIN

AUTHOR: OBIRI N I (Reprint); HUSAIN S R;  
DEBINSKI W; PURI R K  
CORPORATE SOURCE: NIH, LAB MOL TUMOR BIOL,  
DIV CELLULAR & GENE THERAPIES,  
CTR BIOL EVALUAT & RES, HFM-530, BLDG  
29B, BETHESDA, MD,  
20892 (Reprint); US FDA, LAB MOL TUMOR  
BIOL, DIV CELLULAR  
& GENE THERAPIES, CTR BIOL EVALUAT &  
RES, BETHESDA, MD,  
20892; PENN STATE UNIV, COLL MED,  
MILTON S HERSHEY MED  
CTR, DEPT MED, DIV NEUROSURG,  
HERSHEY, PA, 17033  
COUNTRY OF AUTHOR: USA  
SOURCE: CLINICAL CANCER RESEARCH, (OCT  
1996) Vol. 2, No. 10, pp.  
1743-1749.  
ISSN: 1078-0432.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: CLIN  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 32

\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*  
AB Interleukin-13 (IL-13) is a cytokine produced primarily  
by activated T  
lymphocytes. It exerts a variety of effects on different cell  
types,  
including monocytes, B lymphocytes, mast cells, and  
keratinocytes. The  
effects of IL-13 on target cells are often similar to the effects  
of  
\*\*\*IL\*\*\* - \*\*\*\*4\*\*\* , which is another cytokine product  
of activated T  
lymphocytes. We recently described the expression of  
intermediate- to  
high-affinity receptors for IL-13 (IL-13R) on renal cell  
carcinoma (RCC)  
cells. In the present study, we examined the effect of IL-13  
on the growth  
of RCC cells as measured by [H-3]thymidine uptake and a  
clonogenic assay.  
In addition, we used an IL-4R-specific antibody to examine  
the specificity  
of IL-4R and IL-13R binding and function. We observed  
that IL-13 inhibited  
RCC cell proliferation by up to 50% and colony formation  
by up to 32% when  
compared with cells cultured in medium alone. A  
combination of \*\*\*IL\*\*\*  
- \*\*\*\*4\*\*\* and IL-13 did not have an additive or  
synergistic effect on  
the growth of RCC cells. These cells expressed mRNA for  
IL-13 and secreted  
immunoreactive IL-13 protein in culture. The  
growth-inhibitory effects of  
IL-13 were specific, because they were not affected by  
antibodies to IL-4  
or to the 140-kilodalton subunit of IL-4R. Furthermore,  
polyclonal  
antibodies to LL-4R failed to inhibit the binding of  
I-125-IL-13 to RCC  
cells. These results indicate that IL-13 has significant  
antiproliferative  
effects on human RCC cells, and the inhibition of IL-13  
effects by  
anti-IL-4R antibody previously reported in lymphoid cells  
does not occur  
in RCC cells.

L5 ANSWER 72 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 96:629521 SCISEARCH  
THE GENUINE ARTICLE: VC092  
TITLE: STIMULATION OF  
SIGNAL-TRANSDUCTION PATHWAYS IN  
LYMPHOCYTES  
FROM PATIENTS WITH  
X-SCID-ACTIVATION THROUGH THE  
\*\*\*IL\*\*\* - \*\*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
\*\*\*RECEPTOR\*\*\* BUT NOT THE IL-2  
RECEPTOR  
AUTHOR: SMITH S (Reprint); JOHNSTON J; JAHN  
T; PUCK J; OSHEA J;  
WEINBERG K; TAYLOR N  
CORPORATE SOURCE: CHILDRENS HOSP LOS  
ANGELES, DIV IMMUNOL RES, LOS ANGELES,  
CA, 90027; NIAMS, BETHESDA, MD, 00000;  
NIH, NATL CTR HUMAN  
GENOME RES, BETHESDA, MD, 00000  
COUNTRY OF AUTHOR: USA  
SOURCE: EXPERIMENTAL HEMATOLOGY, (AUG  
1996) Vol. 24, No. 9, pp.  
411.  
ISSN: 0301-472X.  
DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: No References

L5 ANSWER 73 OF 82 SCISEARCH COPYRIGHT 2000  
ISI (R)  
ACCESSION NUMBER: 95:292579 SCISEARCH  
THE GENUINE ARTICLE: QU271  
TITLE: ISOLATION OF AN IL-13-DEPENDENT  
SUBCLONE OF THE B9  
CELL-LINE USEFUL FOR THE ESTIMATION  
OF HUMAN IL-13  
BIOACTIVITY  
AUTHOR: LABITTEBOUTEILLER C (Reprint);  
ASTRUC R; MINTY A; FERRARA  
P; LUPKER J H  
CORPORATE SOURCE: SANOFI RECH, CTR LABEGE,  
BP 137, F-31676 LABEGE, FRANCE  
(Reprint)  
COUNTRY OF AUTHOR: FRANCE  
SOURCE: JOURNAL OF IMMUNOLOGICAL  
METHODS, (12 APR 1995) Vol. 181,  
No. 1, pp. 29-36.  
ISSN: 0022-1759.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 20

\*ABSTRACT IS AVAILABLE IN THE ALL  
AND IALL FORMATS\*  
AB A novel sub-clone of the B9 hybridoma cell line  
(B9-1-3) has been  
selected by cloning following continuous culture in rhlL-13.  
This cell  
line shows an increased sensitivity to both hIL-13 and  
mIL-4 compared to  
the parental B9 cell line. The proliferative response to IL-13  
can be  
blocked with an anti- \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor  
monoclonal antibody  
but not with the soluble \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor,  
suggesting  
that IL-13- and \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* -binding receptor  
subunits are  
distinct but form part of a common receptor complex.  
Although the B9-1-3  
cell line is still sensitive to picogrammes of IL-6, it can be  
used to  
measure IL-13 in the presence of IL-6 by inclusion of  
excess neutralizing  
IL-6 antibody. This cell line should thus prove useful both  
in measuring  
the IL-13 bioactivity and for the dissection of the molecular  
nature of  
the IL-13: \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor complex.

L5 ANSWER 74 OF 82 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1999:659425 CAPLUS  
DOCUMENT NUMBER: 131:285412  
TITLE: Mutagenized IL13-based chimeric molecules  
INVENTOR(S): Debinski, Waldemar  
PATENT ASSIGNEE(S): The Penn State Research  
Foundation, USA  
SOURCE: PCT Int. Appl., 57 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.
WO 9951643	A1	19991014	WO 1999-US7188
19990331			
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
AU 9933774	A1	19991025	AU 1999-33774
19990331			
PRIORITY APPLN. INFO.:			US 1998-54711
19980403			
			WO 1999-US7188 19990331
AB	This invention provides mutagenized interleukin 13 mols. that show improved specificity for the restricted ( ***IL4*** independent) ***IL13*** ***receptor*** and reduced cross		

reactivity with the  
\*\*\*IL4\*\*\* / \*\*\*IL4\*\*\* shared receptor. The  
mutagenized IL13 mols.  
include one or more mutations in a domain that interacts  
with the 140 kDa  
hIL4R beta. or the hIL13R.alpha.1 subunit. These  
mutagenized IL13 mols.  
provide effective targeting moieties in chimeric mols. (e.g.  
fusion  
proteins) that specifically deliver effector mols. (e.g.  
cytotoxins) to  
cells overexpressing \*\*\*IL13\*\*\* \*\*\*receptors\*\*\*  
(e.g. cancer cells  
such as gliomas).

L5 ANSWER 75 OF 82 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1999:395927 CAPLUS  
DOCUMENT NUMBER: 131:212694  
TITLE: Signal transduction by cytokines  
AUTHOR(S): Schrader, John W.  
CORPORATE SOURCE: Biomedical Research Centre,  
University of British  
Columbia, Vancouver, BC, V6T 1Z3, Can.  
SOURCE: Signal Transduction Mast Cells Basophils  
(1999),  
66-84. Editor(s): Razin, Ehud; Rivera, Juan.  
Springer: New York, N. Y.  
CODEN: 67UEAX

DOCUMENT TYPE: Conference; General Review  
LANGUAGE: English  
AB A review with 118 refs. Mast cells and cytokines, the  
four-helix bundle  
cytokine family, the cytokine receptor superfamily, ligand  
oligomerization  
of cytokine receptors, interferons and interleukins are some  
of the topics  
discussed. Tyrosine phosphorylation events involving Shc  
as an adaptor,  
MAP kinases, JNK/SAP kinases, SHP-2 tyrosine  
phosphatase, JAK-STAT  
pathway, PI-3 kinase and the activation of Ras proteins in  
mast cell  
activation are some of the events discussed here. The role  
of \*\*\*IL\*\*\*  
- \*\*\*\*4\*\*\* and \*\*\*IL\*\*\* - \*\*\*13\*\*\*  
\*\*\*receptors\*\*\* and the  
differences and similarities in signal transduction by  
different cytokines  
are also summarized.

L5 ANSWER 76 OF 82 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1998:648072 CAPLUS  
DOCUMENT NUMBER: 130:64806  
TITLE: Cytokines and IgE regulation  
AUTHOR(S): Punnonen, Juha; De Vries, Jan E.  
CORPORATE SOURCE: Human Immunology  
Department, DNAX Research Institute  
of Molecular and Cellular Biology, Palo Alto,  
CA, USA  
SOURCE: Allergy Allerg. Dis. (1998), 13-40.  
Editor(s): Denburg, Judah A. Humana: Totowa, N. J.  
CODEN: 66UHAZ

DOCUMENT TYPE: Conference; General Review  
LANGUAGE: English  
AB A review with 226 refs. of the mol. and biol. properties of  
interleukin-4  
and interleukin-13, as well as the effects of other cytokines  
on the  
\*\*\*IL\*\*\* - \*\*\*\*4\*\*\* - and IL-13-induced IgE formation.  
In addn., the  
authors discuss recently characterized \*\*\*IL\*\*\* -  
\*\*\*\*4\*\*\* and  
\*\*\*IL\*\*\* - \*\*\*13\*\*\* \*\*\*receptor\*\*\* antagonists as  
possible means  
to block \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* - and IL-13-induced IgE  
synthesis in  
atopic individuals.

L5 ANSWER 77 OF 82 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1998:480562 CAPLUS  
DOCUMENT NUMBER: 129:147990  
TITLE: The signal transduction mechanism of  
\*\*\*IL\*\*\*  
- \*\*\*\*4\*\*\* in X-linked severe combined  
immunodeficiency  
patients  
AUTHOR(S): Izuhara, Kenji  
CORPORATE SOURCE: Department Human Genetics,  
National Institute  
Genetics, Japan  
SOURCE: Asahi Garasu Zaidan Josei Kenkyu Seika  
Hokoku (1997)  
No pp. given  
CODEN: AGSHEN; ISSN: 0919-9179  
URL:  
<http://www.af-info.or.jp/IPN/subsidy/report2/1998/body/97A-C15-P050.TXT>  
PUBLISHER: Asahi Garasu Zaidan  
DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: Japanese  
 AB Both interleukin 4 ( \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* ) and IL-13 are pleiotropic cytokines, and have similar biol. activities with each other. The \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor is assumed to be composed of the \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor .alpha. chain (IL-4R.alpha.) and the IL-2 receptor .gamma. chain (gamma.c), and the \*\*\*IL\*\*\* - \*\*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* is assumed to be composed of the \*\*\*IL\*\*\* - \*\*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* .alpha. chain and IL-4R.alpha., resp. To clarify the signal transduction mechanisms of these two cytokines, we analyzed those in B cells derived from X-linked severe combined immunodeficiency patients, in which there exist genetic abnormalities on the gamma.c gene. Consequently, both a tyrosine kinase, JAK3, and a transcription factor, STAT6, which are known to be activated by \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* in normal B cells, were not activated in patients' B cells. These results suggest that there is a cascade of .gamma.c/JAK3/STAT6 in the signal pathway of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*. On the other hand, the finding that STAT6 was activated by IL-13 even in patients' cells suggest that IL-13R does not utilize .gamma.c.

L5 ANSWER 78 OF 82 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1997:270246 CAPLUS  
 DOCUMENT NUMBER: 127:62254  
 TITLE: A novel 4-kb interleukin-13 receptor .alpha. mRNA

expressed in human B, T, and endothelial cells encoding an alternate type-II interleukin-4/interleukin-13 receptor

AUTHOR(S): Gauchat, Jean Francois; Schlangerhauf, Edith; Feng,

Ning Ping; Moser, Rene; Yamage, Mat; Jearnir, Pascale;

Alouani, Sami; Elson, Greg; Notarangelo, Luigi D.;

Wells, Timothy; Eugster, Hans Pietro; Bonnefoy, Jean

Yves  
 CORPORATE SOURCE: Geneva Biomedical Research Institute, Glaxo Wellcome

Research Development S. A., Plan-les-Quates, CH-1228,

Switz.

SOURCE: Eur. J. Immunol. (1997), 27(4), 971-978  
 CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: VCH  
 DOCUMENT TYPE: Journal

LANGUAGE: English  
 AB A 4 kb human interleukin-13 receptor (IL-13R) chain cDNA was cloned from a

B cell cDNA library using expressed sequence tags homologous to mouse

IL-13R as probes. The deduced protein sequence shows a significant level

of sequence identity with the IL-5R and the human IL-13R identified

recently by expression cloning. The cytoplasmic region is very highly

conserved between human and mouse homologs and contains a consensus

binding motif for a signal transducer and activator of transcription. The

cDNA encodes a protein binding IL-13 when expressed alone which

participates in a receptor complex for both \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and

IL-13 when expressed in conjunction with the IL-4R.alpha. chain.

Transcripts for this IL-13R chain could be detected in most tissues and

organs studied and in T, B, endothelial cells, basophilic, immature mast

cell, and monocytic cell lines. The pattern of expression is different

from the other recently cloned IL-13R mol., and correlates with sites

where \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 signaling is known to occur.

This novel receptor is likely to be implicated in reactions involved in

IgE responses, T helper 2 differentiation, adhesion of leukocytes to

endothelium, and in pathol. phenomena such as allergy, atopy, and asthma.

L5 ANSWER 79 OF 82 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:69036 CAPLUS  
 DOCUMENT NUMBER: 126:170067  
 TITLE: Control of IgE antibody production by drug  
 AUTHOR(S): Yanagihara, Yukiyo  
 CORPORATE SOURCE: Natl. Sagami Hosp., Sagami, 228, Japan  
 SOURCE: Aterugi no Ryoiki (1995), Volume Date 1996, 3(1),

13-18  
 CODEN: ARRYFB; ISSN: 1340-2358

PUBLISHER: Iyaku Janarusha  
 DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese  
 AB A review with 10 refs. on roles of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* /IL-13,

\*\*\*IL\*\*\* - \*\*\*\*4\*\*\* / \*\*\*IL\*\*\* - \*\*\*\*13\*\*\*

\*\*\*receptor\*\*\*, and CD40/CD40L in IgE prodn. and inhibitors for IgE prodn. such as

immunosuppressants (CsA and FK506), glucocorticoids, gangliosides,

IPD-1151T (sulplast tosilate), DSCG (disodium cromoglycate), IgE binding

mols., and cytokines.

L5 ANSWER 80 OF 82 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1996:578319 CAPLUS  
 DOCUMENT NUMBER: 125:325421

TITLE: Modulation of the human IgE response  
 AUTHOR(S): De Vries, J. E.; Yssel, H.

CORPORATE SOURCE: Human Immunology Dept, DNAX Research Institute

Molecular and Cellular Biology, Palo Alto, CA, 94304,

USA

SOURCE: Eur. Respir. J. (1996), 9(Suppl. 22), S85-62S

CODEN: ERJOEJ; ISSN: 0903-936

DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English

AB A review with 35 refs. Studies on the immunol. basis of allergic diseases

have indicated that enhanced prodn. of the cytokines interleukin (

\*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 and the reduced prodn. of

interferon-gamma (IFN-gamma.) by allergen-specific T-cells contribute

to enhanced IgE synthesis and the development of allergic disease in

certain individuals. Therefore, inhibition of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\*

and IL-13 synthesis or blocking of activities of these cytokines would be

one approach to inhibiting IgE prodn. In the present communication, novel

approaches toward this goal are discussed. It is shown that an \*\*\*IL\*\*\*

- \*\*\*\*4\*\*\* mutant protein, in which the tyrosine residue at position 124

is replaced by aspartic acid ( \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* .Y124D), binds with

high affinity to the \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* receptor, without receptor

activation. \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* .Y124D acts as a potent antagonist

both of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and IL-13 activity in vitro, and inhibits

IgG4 and IgE prodn. induced by these cytokines. These data are compatible

with the notion that the \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and \*\*\*IL\*\*\*

- \*\*\*\*13\*\*\*  
 \*\*\*receptors\*\*\* are complex receptors, which share a common

component, which is required for signal transduction. In addn., it has

been demonstrated that allergen-specific T-cells, belonging to the

T-helper 2 (Th2) subset can be rendered anergic after incubation with

allergen-derived peptides representing minimal T-cell activation inducing

epitopes. These anergic Th2 cells failed to produce \*\*\*IL\*\*\*

- \*\*\*\*4\*\*\* and IL-13, and failed to proliferate after activation with

allergen and antigen-presenting cells (APC). The anergized T cells also

failed to give B-cells help in IgE synthesis, although they expressed

normal levels of the CD40 ligand (CD40L). Exogenous \*\*\*IL\*\*\*

- \*\*\*\*4\*\*\* or IL-13 failed to restore IgE synthesis, indicating that in

addn. to CD40L other co-stimulatory signals are required for productive

T-cell/B-cell interactions, resulting in IgE synthesis. IgE prodn. was

restored by exogenous IL-2, demonstrating that IL-2 reverses the

nonresponsive state and helper function of these nonresponsive T-cells.

It is tempting to speculate that induction of T-cell nonresponsiveness by

allergen-derived peptides may represent the underlying mechanisms for

successful immunotherapy in allergic patients.

L5 ANSWER 81 OF 82 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97302046 EMBASE  
 DOCUMENT NUMBER: 1997302046

TITLE: A murine interleukin-4 mutant protein (QY) acts as a highly

efficient \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* and \*\*\*IL\*\*\*

- \*\*\*\*13\*\*\*  
 \*\*\*receptor\*\*\* antagonist.

AUTHOR: Grunewald S.; Werthmann A.; Schnarr B.; Sebald W.; Duschl

A.  
 CORPORATE SOURCE: S. Grunewald, Biozentrum, Physiological Chemistry II,

University of Wurzburg, Wurzburg, Germany  
 SOURCE: Immunobiology, (1997) 197/2-4 (203).

Refs: 1  
 ISSN: 0171-2985 CODEN: ZIMMDO

COUNTRY: Germany  
 DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation

029 Clinical Biochemistry  
 030 Pharmacology

037 Drug Literature Index  
 LANGUAGE: English

L5 ANSWER 82 OF 82 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95000814 EMBASE  
 DOCUMENT NUMBER: 1995000814

TITLE: Interleukin 4.

AUTHOR: Banchemau J.  
 CORPORATE SOURCE: Schering-Plough, Lab for Immunological Research, 27 Chemin

des Peupliers, 69572 Dardilly, France  
 SOURCE: FORUM - Trends in Experimental and Clinical Medicine,

(1994) 4/5 (514-531).

ISSN: 1121-8142 CODEN: FTCME2

COUNTRY: Italy  
 DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

026 Immunology, Serology and Transplantation  
 030 Pharmacology

037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB Human interleukin 4 ( \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* ), a mature 129 amino acid

(AA) glycoprotein secreted by activated T cells and basophils, is a

pleiotropic cytokine that affects T and B lymphocytes, monocytes,

dendritic cells, polymorphonuclear cells, fibroblasts, endothelial cells

and hepatocytes. It may display contrasting biological effects according

to the differentiation stage of a given cell and to the cytokine environment. \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* is a growth factor for

activated T

and B cells, and both in vivo and in vitro studies have shown the crucial

role of \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* in the induction of immunoglobulin E

production. \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* 's ability in inducing naive T helper

cells to differentiate into \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* secreting Th2 cells

is critical. \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* inhibits, in vitro and in vivo, the

secretion of proinflammatory cytokines by monocytes/macrophages and

polymorphonuclears. Human \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* binds to a high

affinity receptor which is composed of at least a 130-kD glycoprotein of

800 AA and a .gamma. chain common to the IL-2, IL-7 and \*\*\*IL\*\*\*

- \*\*\*\*13\*\*\*  
 \*\*\*receptors\*\*\* . \*\*\*IL\*\*\* - \*\*\*\*4\*\*\* may prove useful

as an antitumoural and anti-inflammatory agent.